#3

FIG. 1A

```
1    agggagaggc agtgaccatg aaggctgtgc tgcttgccct gttgatggca
51   ggcttggccc tgcagccagg cactgccctg ctgtgctact cctgcaaagc
101  ccaggtgagc aacgaggact gcctgcaggt ggagaactgc acccagctgg
151  gggagcagtg ctggaccgcg cgcatccgcg cagttggcct cctgaccgtc
201  atcagcaaag gctgcagctt gaactgcgtg gatgactcac aggactacta
251  cgtgggcaag aagaacatca cgtgctgtga caccgacttg tgcaacgcca
301  gcggggccca tgccctgcag ccggctgccg ccatccttgc gctgctccct
351  gcactcggcc tgctgctctg gggacccggc cagctatagg ctctgggggg
401  ccccgctgca gcccacactg ggtgtggtgc cccaggcctt tgtgccactc
451  ctcacagaac ctggcccagt gggagcctgt cctggttcct gaggcacatc
501  ctaacgcaag tttgaccatg tatgtttgca ccccttttcc ccnaaccctg
551  accttcccat gggccttttc caggattccn accnggcaga tcagttttag
601  tganacanat ccgcntgcag atggcccctc caaccntttn tgttgntgtt
651  tccatggccc agcatttcc acccttaacc ctgtgttcag gcacttnttc
701  ccccaggaag ccttccctgc ccaccccatt tatgaattga gccaggtttg
751  gtccgtggtg tcccccgcac ccagcagggg acaggcaatc aggagggccc
801  agtaaaggct gagatgaagt ggactgagta gaactggagg acaagagttg
851  acgtgagttc ctgggagttt ccagagatgg ggcctggagg cctggaggaa
901  ggggccaggc ctcacatttg tggggntccc gaatggcagc ctgagcacag
951  cgtaggccct taataaacac ctgttggata agccaaaaaa aaaaaaaa
```

FIG. 1B

MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQV
ENCTQLGEQCWTARIRAVGLLTVISKGCSLNCVDDS
QDYYVGKKNITCCDTDLCNASGAHALQPAAAILALLPAL
GLLLWGPGQL

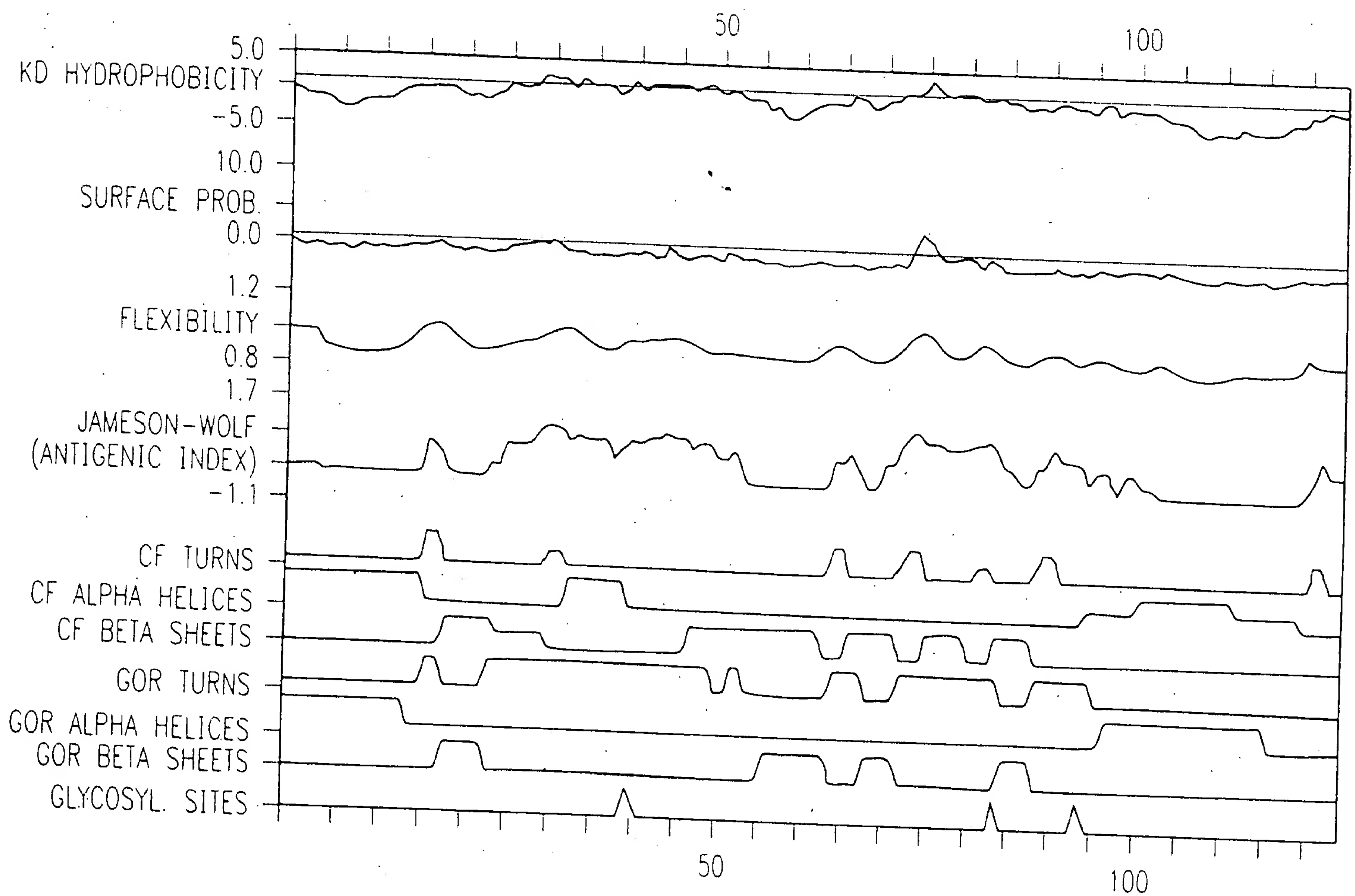
FIG. 2

```
     ATGAAGACAGTTTTTTTTATCCTGCTGGCCACCTACTTAGCCCTGCATCCAGGTGCTGCT
   1 ---------+---------+---------+---------+---------+---------+ 60
     TACTTCTGTCAAAAAAAATAGGACGACCGGTGGATGAATCGGGACGTAGGTCCACGACGA

     M  K  T  V  F  F  I  L  L  A  T  Y  L  A  L  H  P  G  A  A

     CTGCAGTGCTATTCATGCACAGCACAGATGAACAACAGAGACTGTCTGAATGTACAGAAC
  61 ---------+---------+---------+---------+---------+---------+ 120
     GACGTCACGATAAGTACGTGTCGTGTCTACTTGTTGTCTCTGACAGACTTACATGTCTTG

     L  Q  C  Y  S  C  T  A  Q  M  N  N  R  D  C  L  N  V  Q  N

     TGCAGCCTGGACCAGCACAGTTGCTTTACATCGCGCATCCGGGCCATTGGACTCGTGACA
 121 ---------+---------+---------+---------+---------+---------+ 180
     ACGTCGGACCTGGTCGTGTCAACGAAATGTAGCGCGTAGGCCCGGTAACCTGAGCACTGT

     C  S  L  D  Q  H  S  C  F  T  S  R  I  R  A  I  G  L  V  T

     GTTATCAGTAAGGGCTGCAGCTCACAGTGTGAGGATGACTCGGAGAACTACTATTTGGGC
 181 ---------+---------+---------+---------+---------+---------+ 240
     CAATAGTCATTCCCGACGTCGAGTGTCACACTCCTACTGAGCCTCTTGATGATAAACCCG

     V  I  S  K  G  C  S  S  Q  C  E  D  D  S  E  N  Y  Y  L  G

     AAGAAGAACATCACGTGCTGCTACTCTGACCTGTGCAATGTCAACGGGGCCCACACCCTG
 241 ---------+---------+---------+---------+---------+---------+ 300
     TTCTTCTTGTAGTGCACGACGATGAGACTGGACACGTTACAGTTGCCCCGGGTGTGGGAC

     K  K  N  I  T  C  C  Y  S  D  L  C  N  V  N  G  A  H  T  L

     AAGCCACCCACCACCCTGGGGCTGCTGACCGTGCTCTGCAGCCTGTTGCTGTGGGGCTCC
 301 ---------+---------+---------+---------+---------+---------+ 360
     TTCGGTGGGTGGTGGGACCCCGACGACTGGCACGAGACGTCGGACAACGACACCCCGAGG

     K  P  P  T  T  L  G  L  L  T  V  L  C  S  L  L  L  W  G  S

     AGCCGTCTGTAGGCTCTGGGAGAGCCTACCATAGCCCGATTGTGAAGGGATGAGCTGCAC
 361 ---------+---------+---------+---------+---------+---------+ 420
     TCGGCAGACATCCGAGACCCTCTCGGATGGTATCGGGCTAACACTTCCCTACTCGACGTG

     S  R  L  *

     TCCACCCCACCCCCACACAGG
 421 ---------+---------+- 441
     AGGTGGGGTGGGGGTGTGTCC
```

FIG. 3

```
1   M K I F L P V L L A A L L G V E R A S S     hSCA-2
1   M K A V L L A L L M A G L A L Q P G T A     hPSCA
1   M K T V L F L L L A T Y L A L H P G A A     mPSCA

21  L M C F S C L N Q K S N* L Y C L K P T I
21  L L C Y S C K A Q V S N* E D C L Q V E N*
21  L Q C Y S C T A Q M N N* R D C L N V Q N*

41  C S D Q D N Y C V T V S A S A G I G N L
41  C T Q L G E Q C W T A R I R A V G L L T
41  C S L D Q H S C F T S R I R A I G L V T

61  V T F G H S L S K T C S P A C P I P E G
61  V - - - - - - I S K G C S L N C V D D S Q
61  V - - - - - - I S K G C S S Q C E D D S E

81  V N V G V A S M G I S C C Q S F L C N* F
76  D Y Y V G K K - N* I T C C D T D L C N* A
76  N Y Y L G K K - N* I T C C Y S D L C N* V

101 S A A D G G L R A S V T L L G A G L L L
95  S G A H A L Q P A A A I L A L L P A L G
95  N G A H T L K P P T T L G L L T V L C S

121 S L L P A L L R F G P
115 L L L W G P G Q L - -
115 L L L W G S S R L - -
```

FIG. 4



HYDROPHOBICITY PLOT OF PSCA

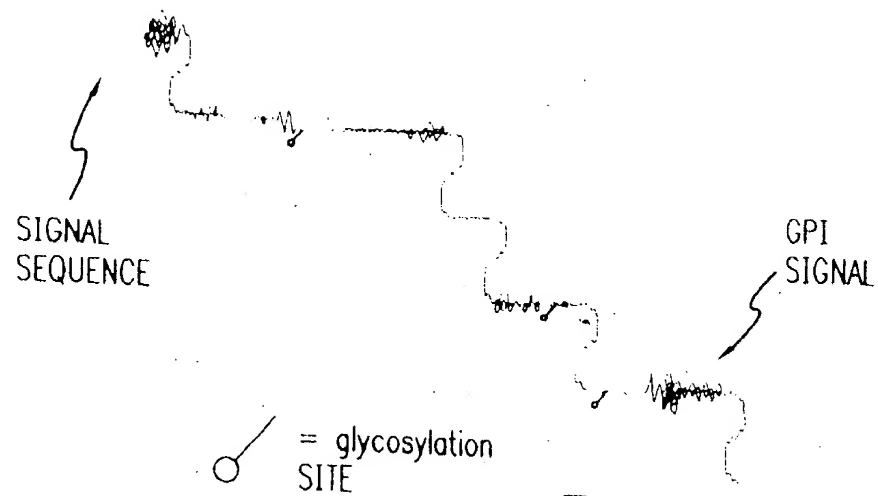

SIGNAL
SEQUENCE
GPI
SIGNAL
= glycosylation
SITE

FIG. 5

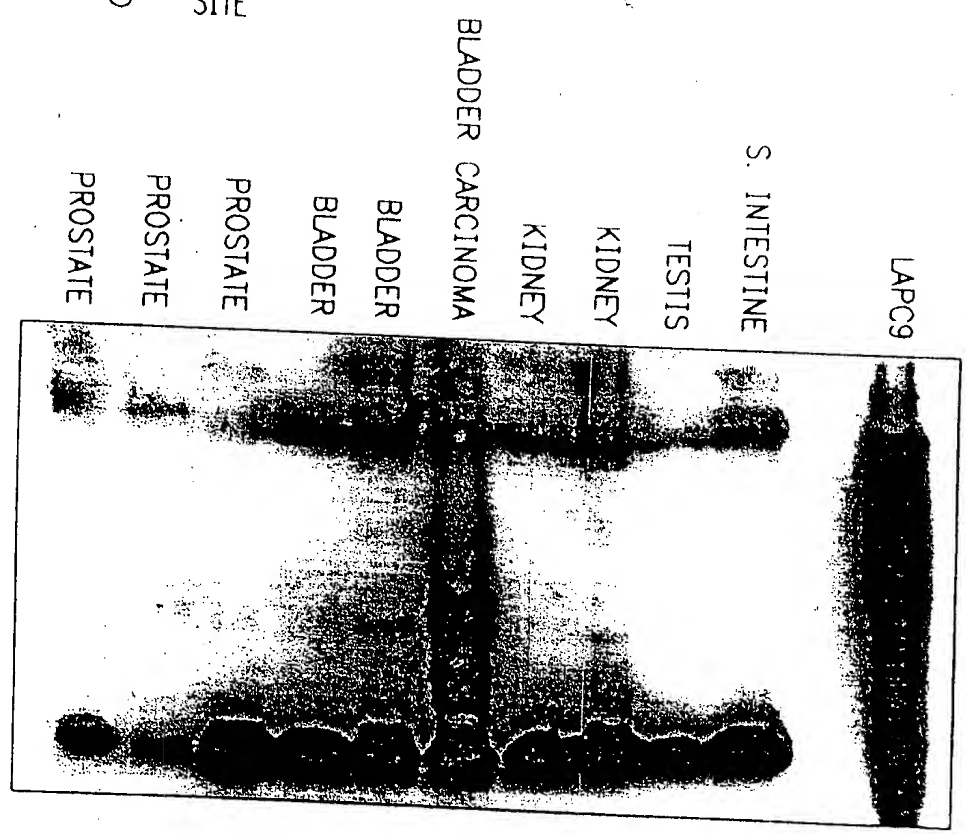

PROSTATE
PROSTATE
PROSTATE
BLADDER
BLADDER
BLADDER CARCINOMA
KIDNEY
KIDNEY
TESTIS
S. INTESTINE
LAPC9

FIG. 6

09855632.100901

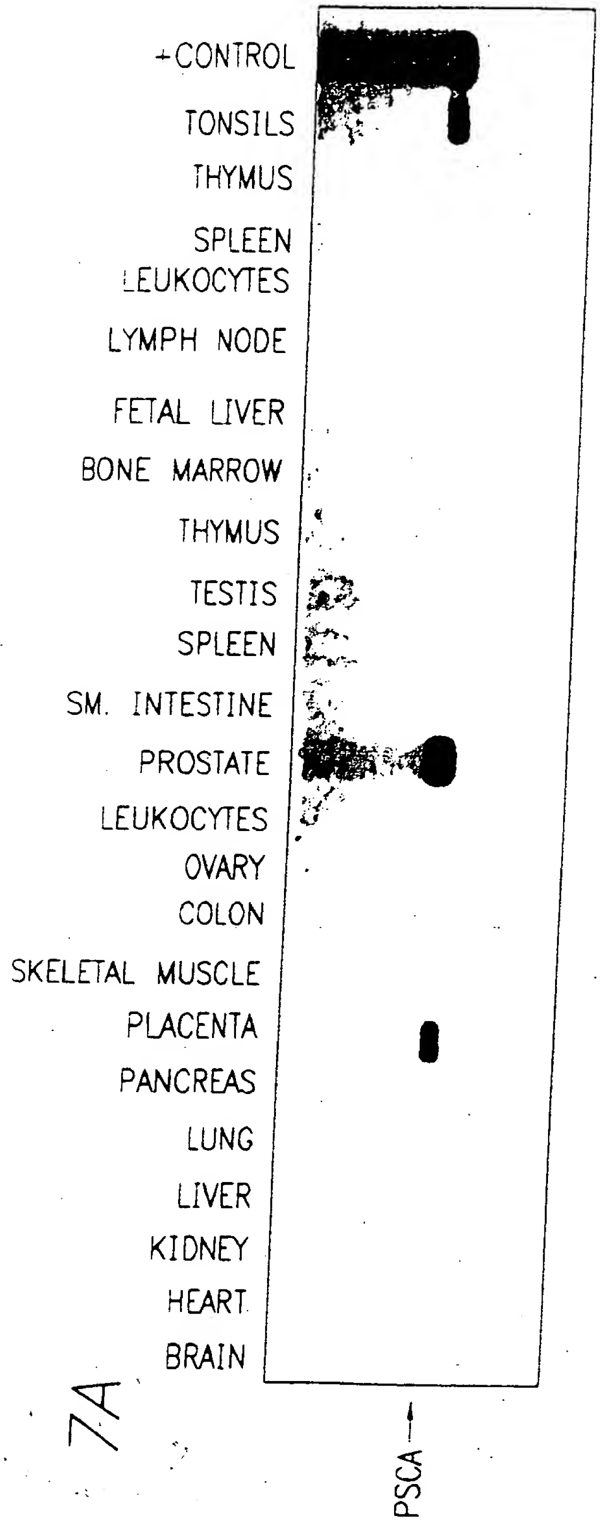


FIG. 7A

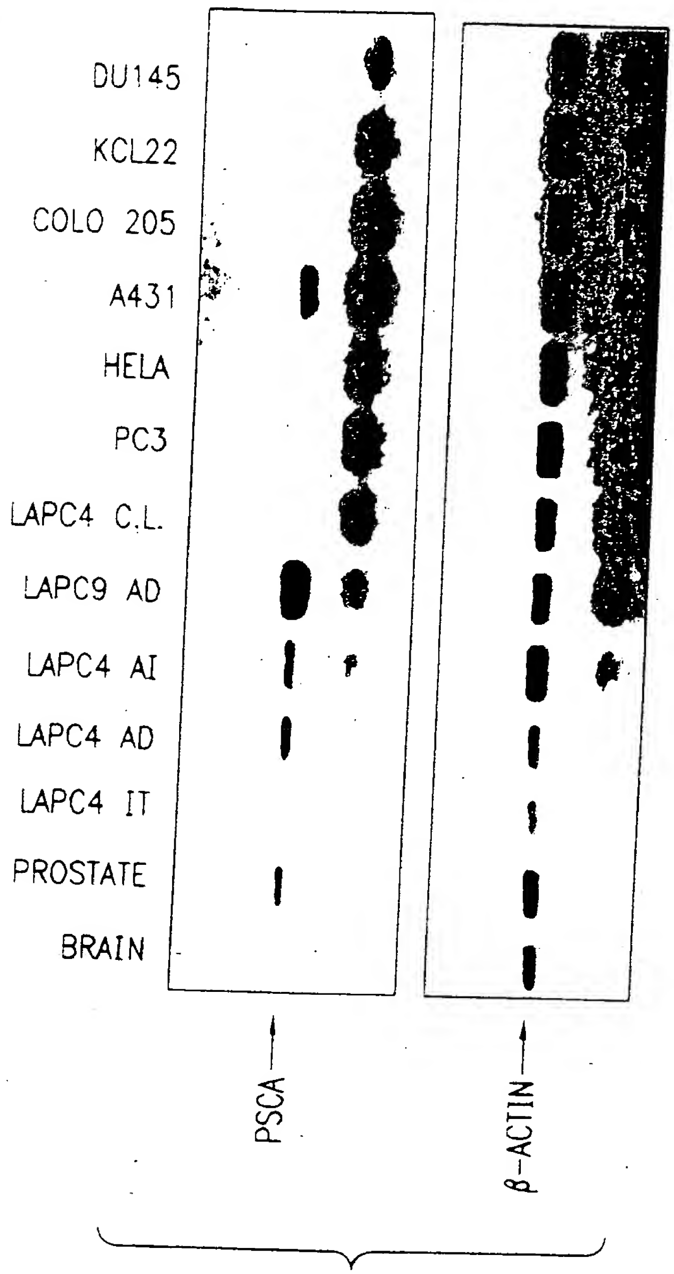


FIG. 7B

FIG. 8A

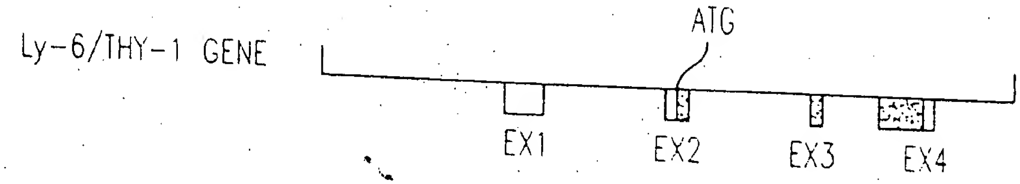


FIG. 8B

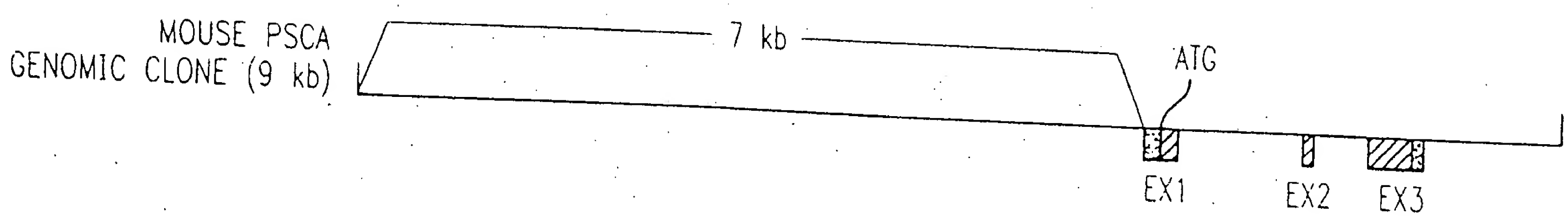
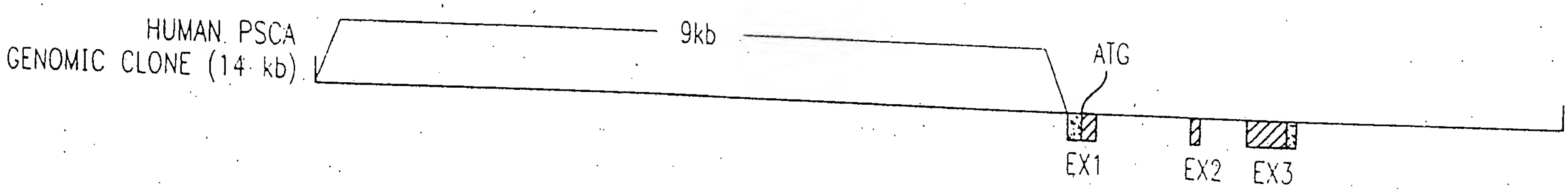


FIG. 8C



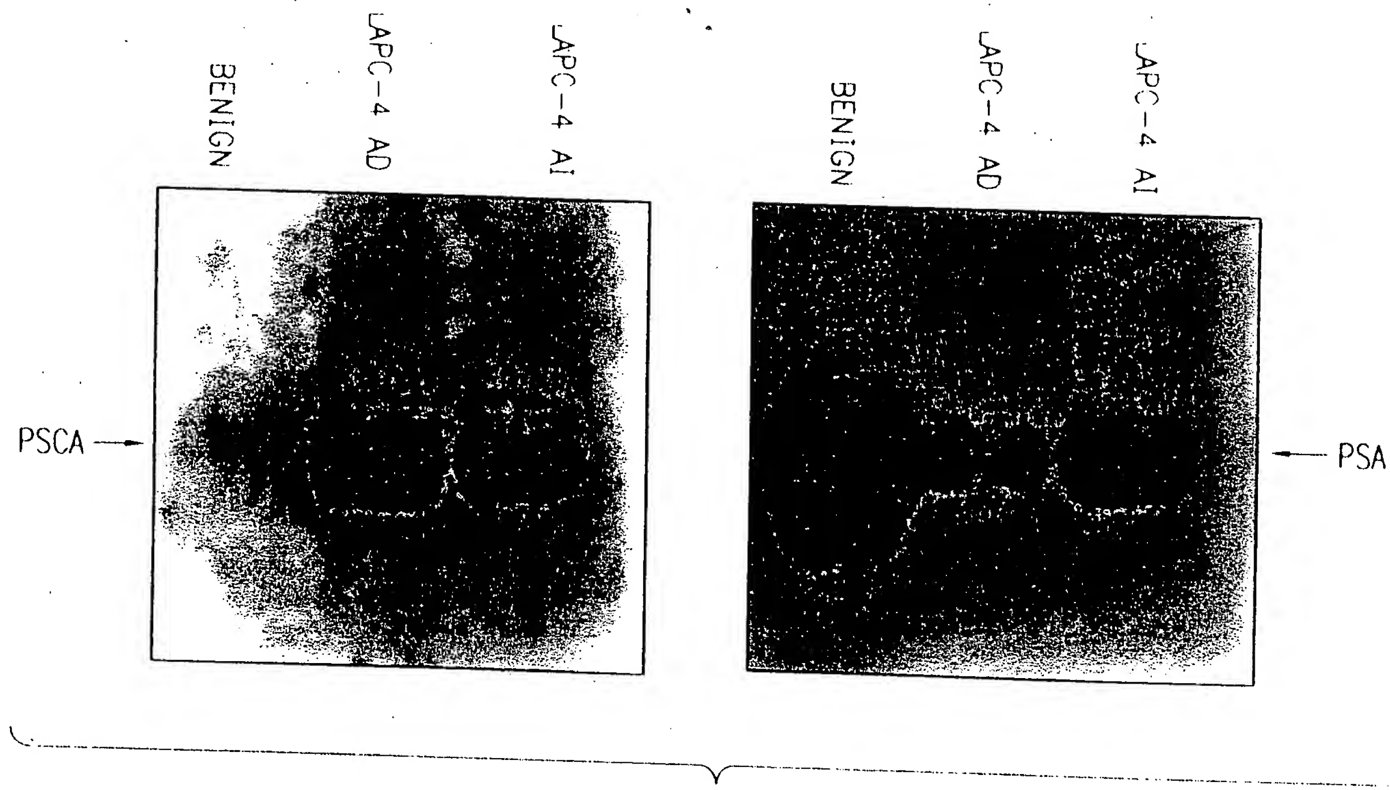


FIG. 9A

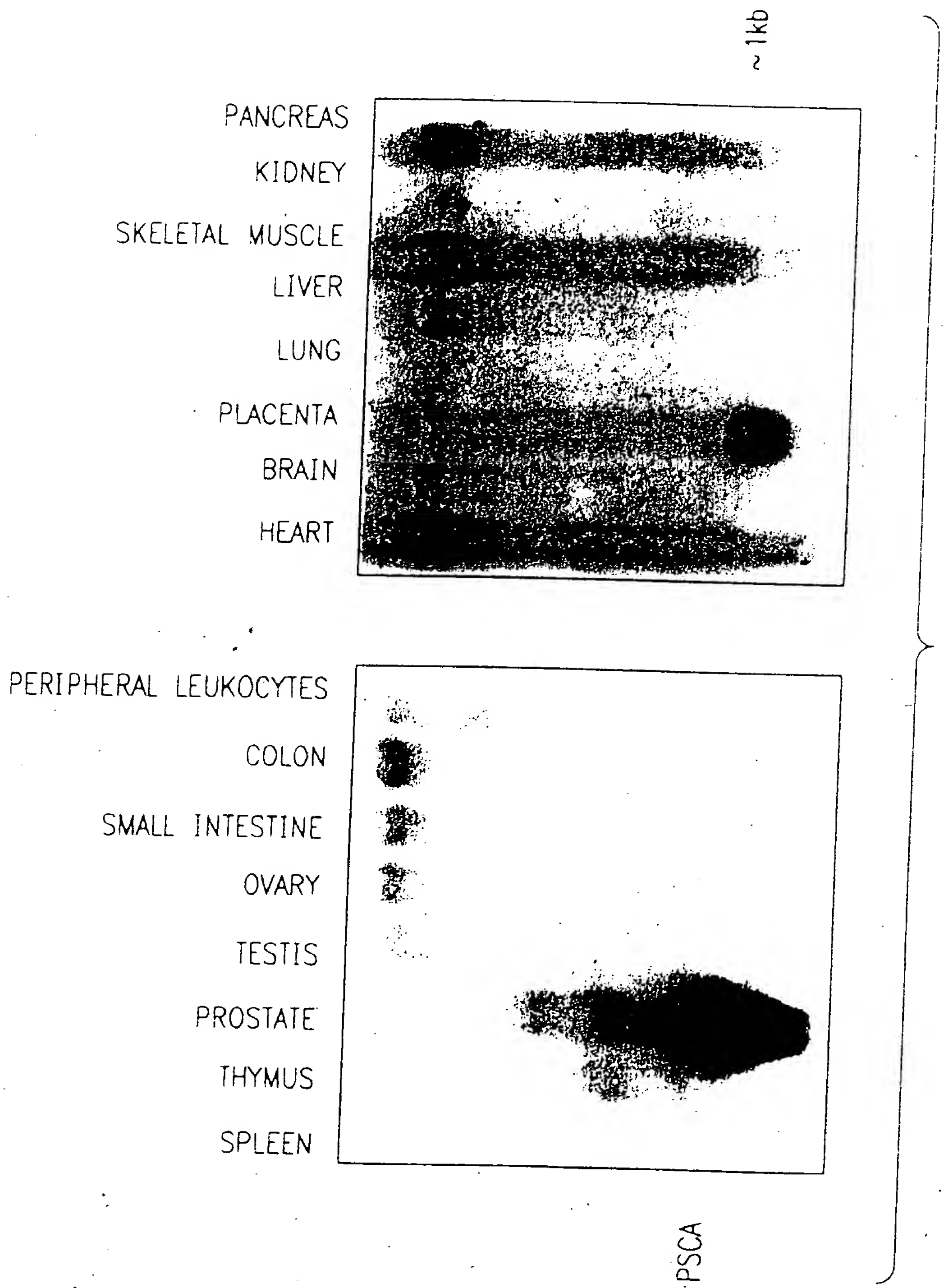

~1kb
PANCREAS
KIDNEY
SKELETAL MUSCLE
LIVER
LUNG
PLACENTA
BRAIN
HEART
PERIPHERAL LEUKOCYTES
COLON
SMALL INTESTINE
OVARY
TESTIS
PROSTATE
THYMUS
SPLEEN
PSCA

FIG. 9B

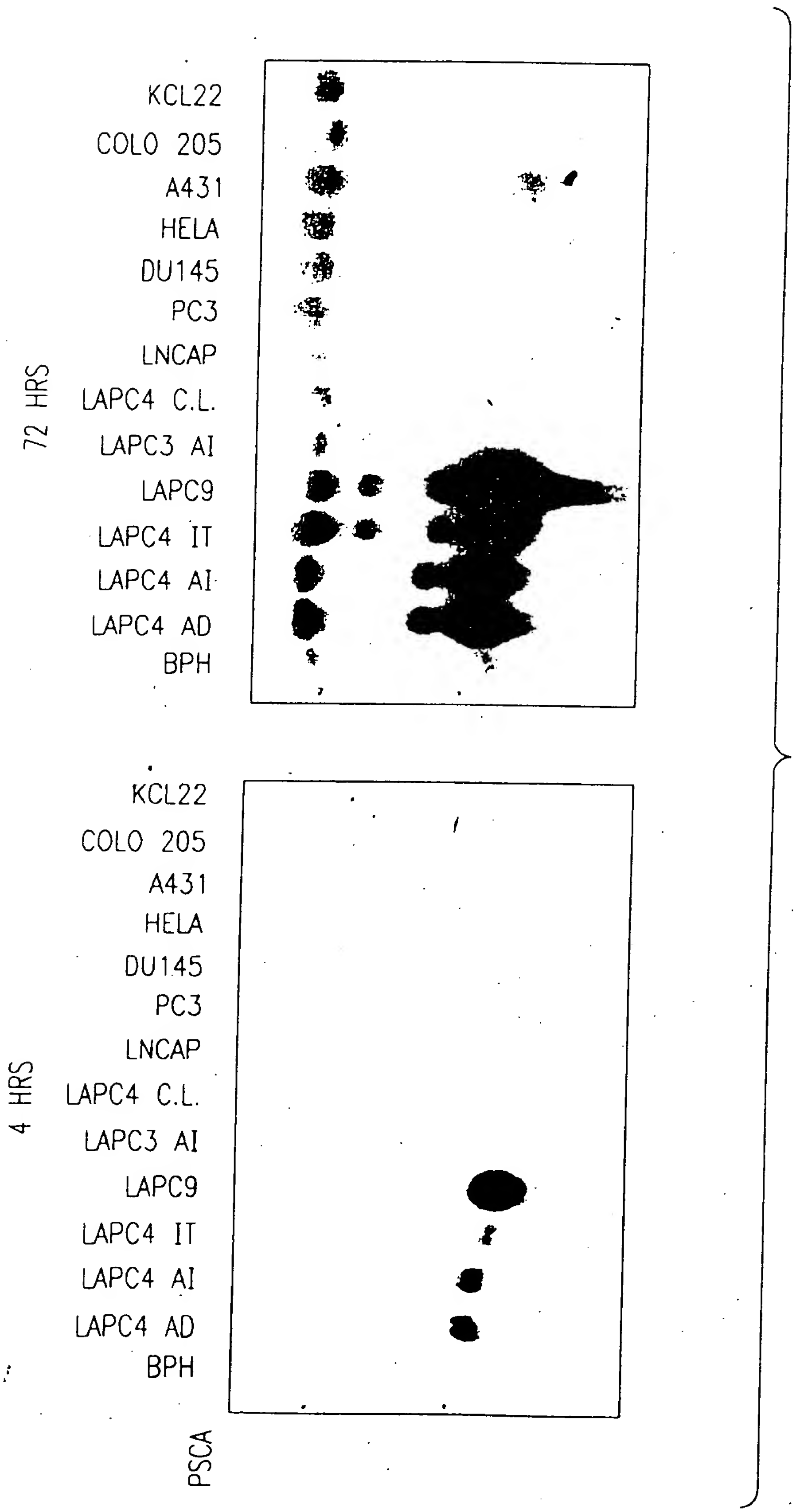

72 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
4 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
PSCA

FIG. 10A

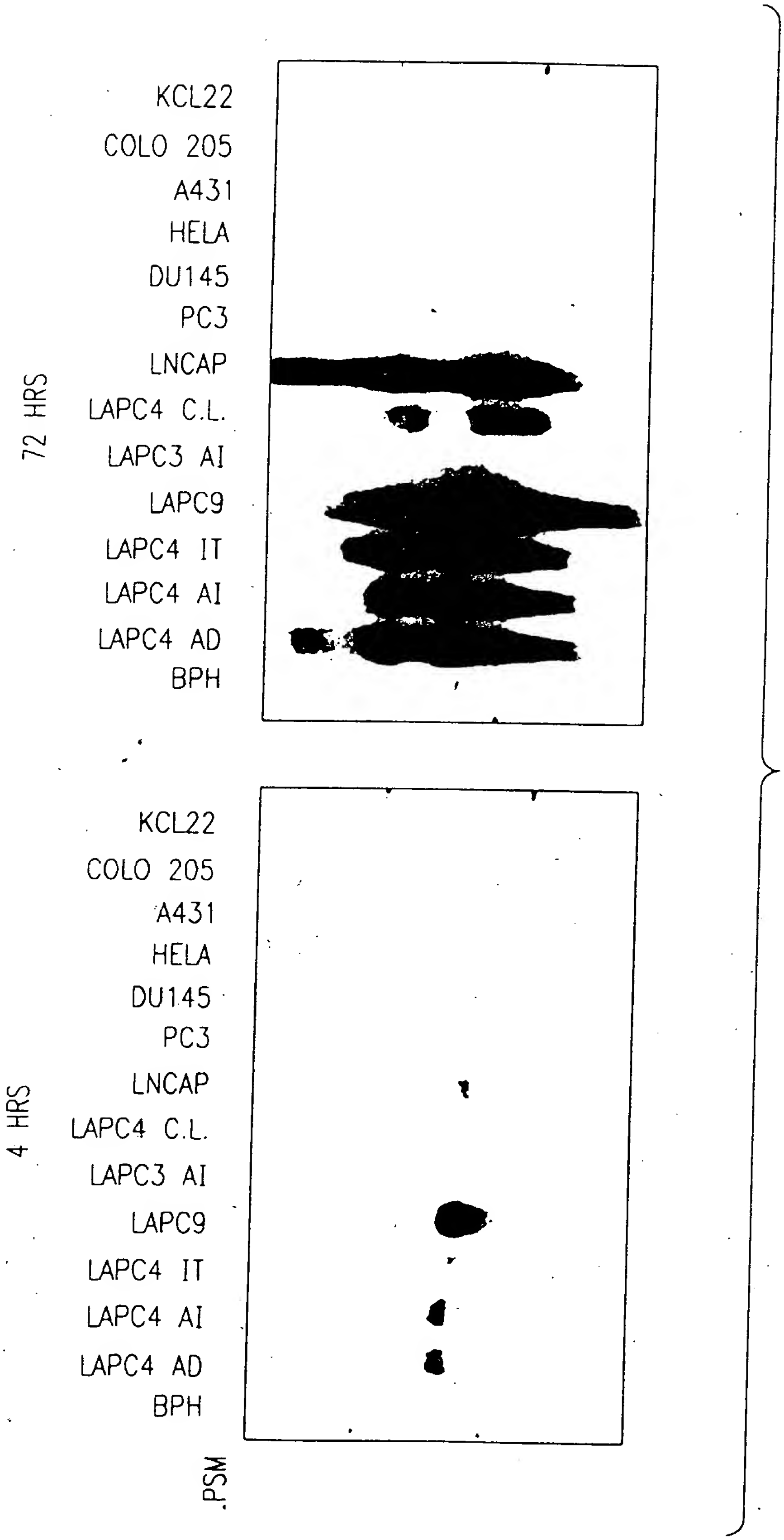

72 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
4 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
PSM

FIG. 10B

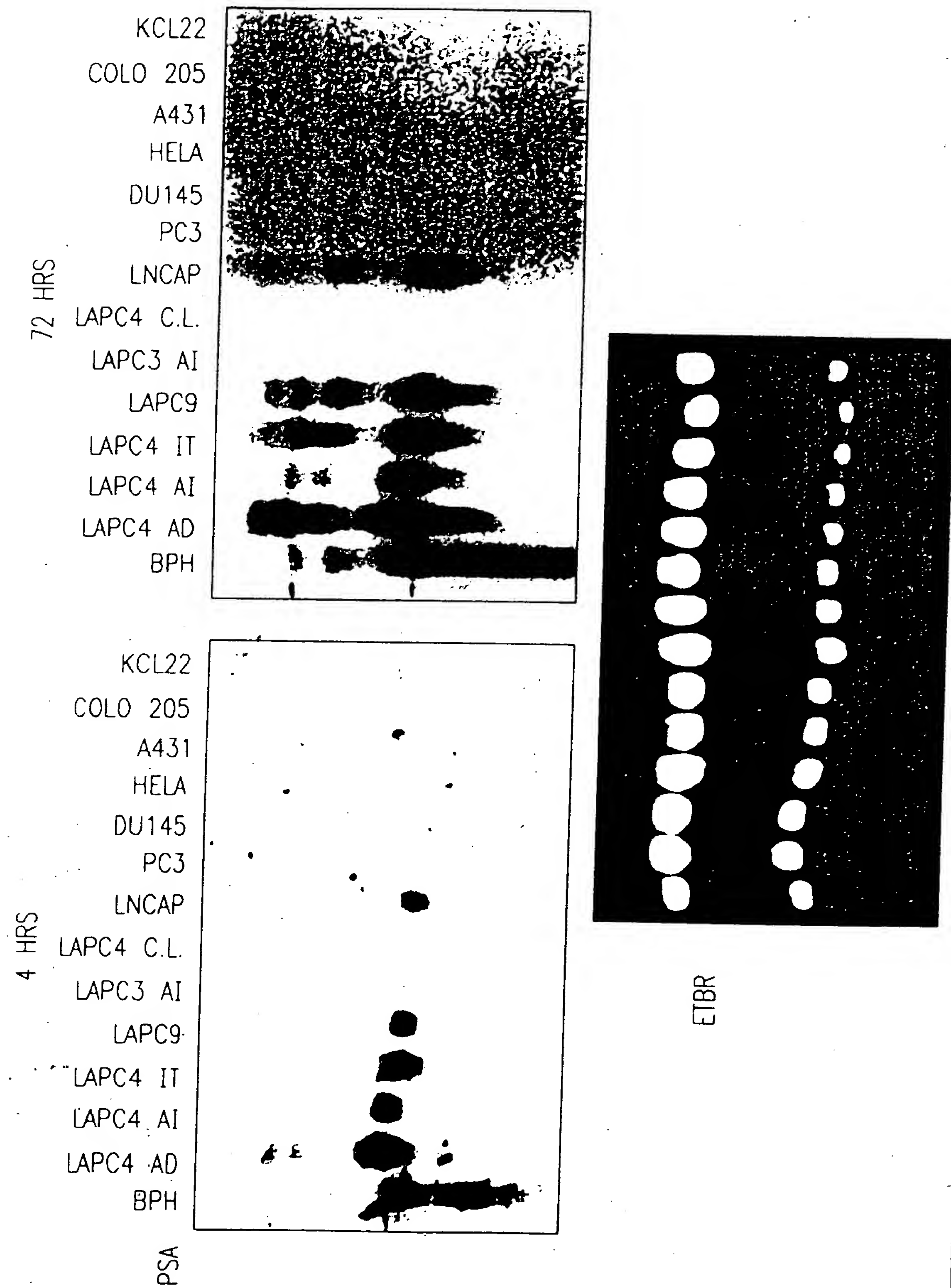

72 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
4 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
PSA
ETBR

FIG. 10C

FIG. 11A

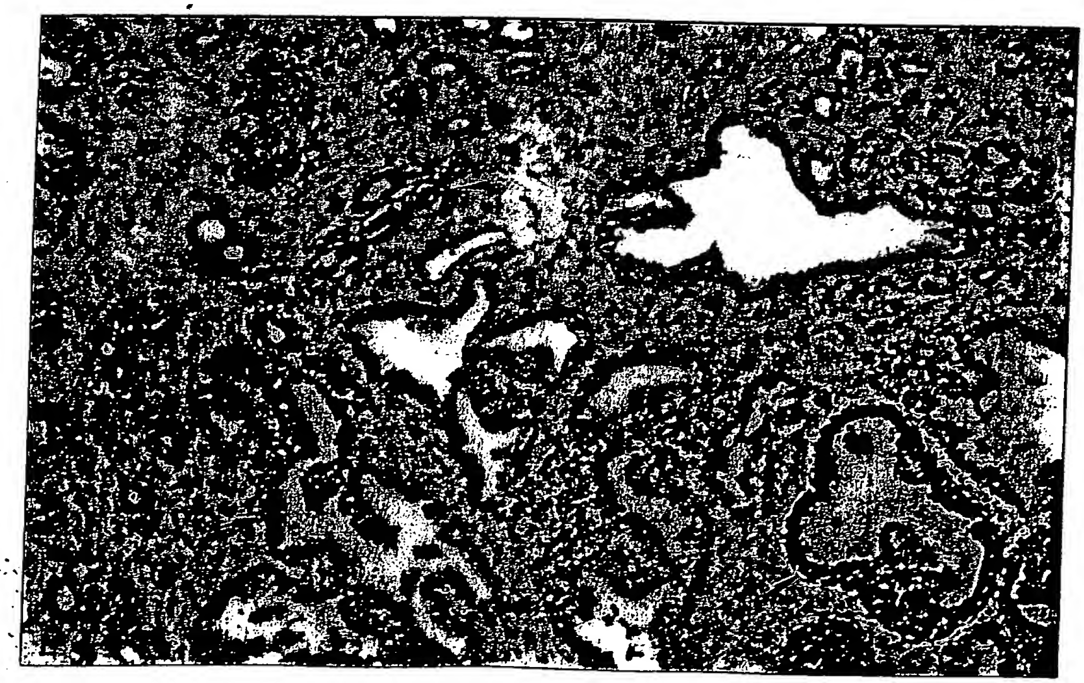


FIG. 11B

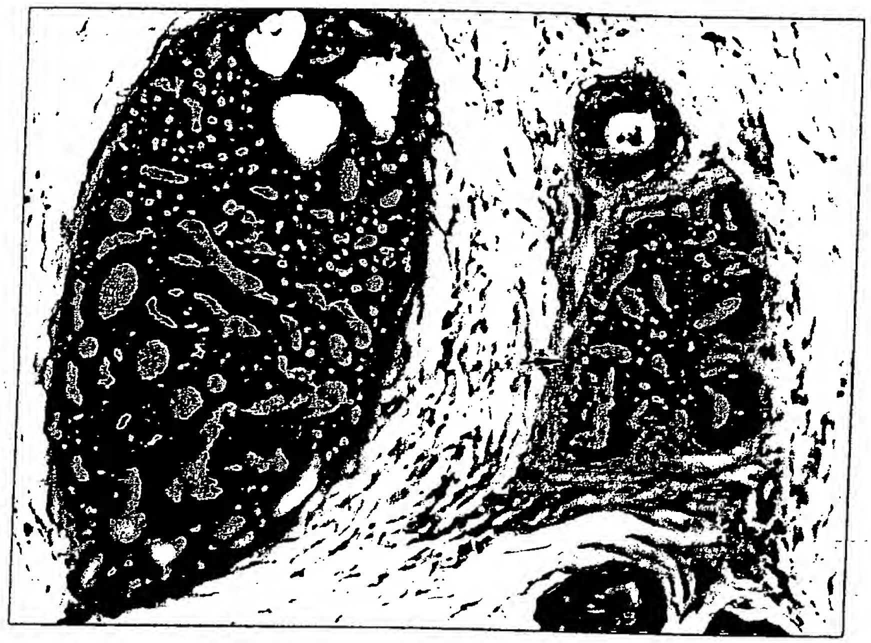


FIG. 11C

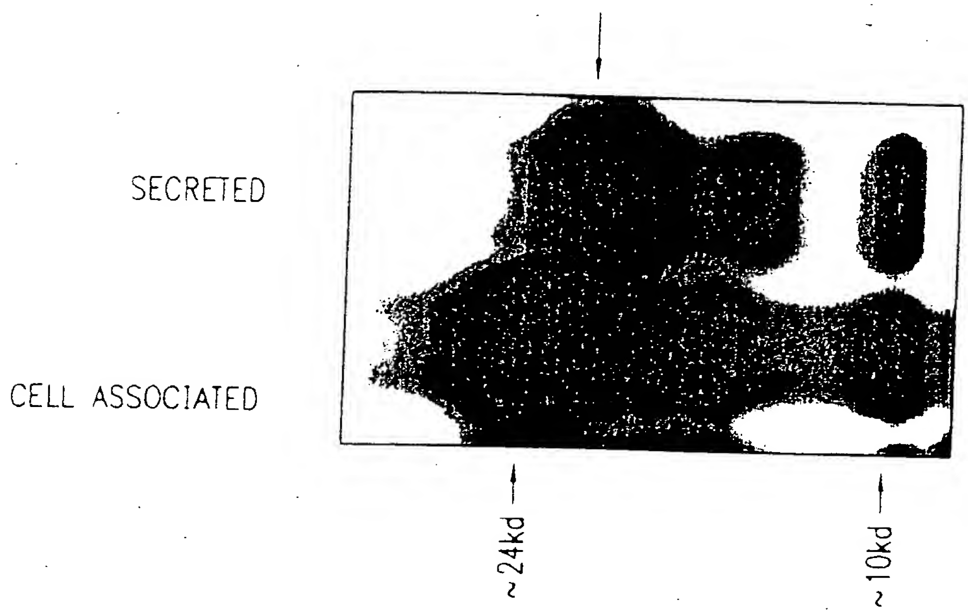


FIG. 12B

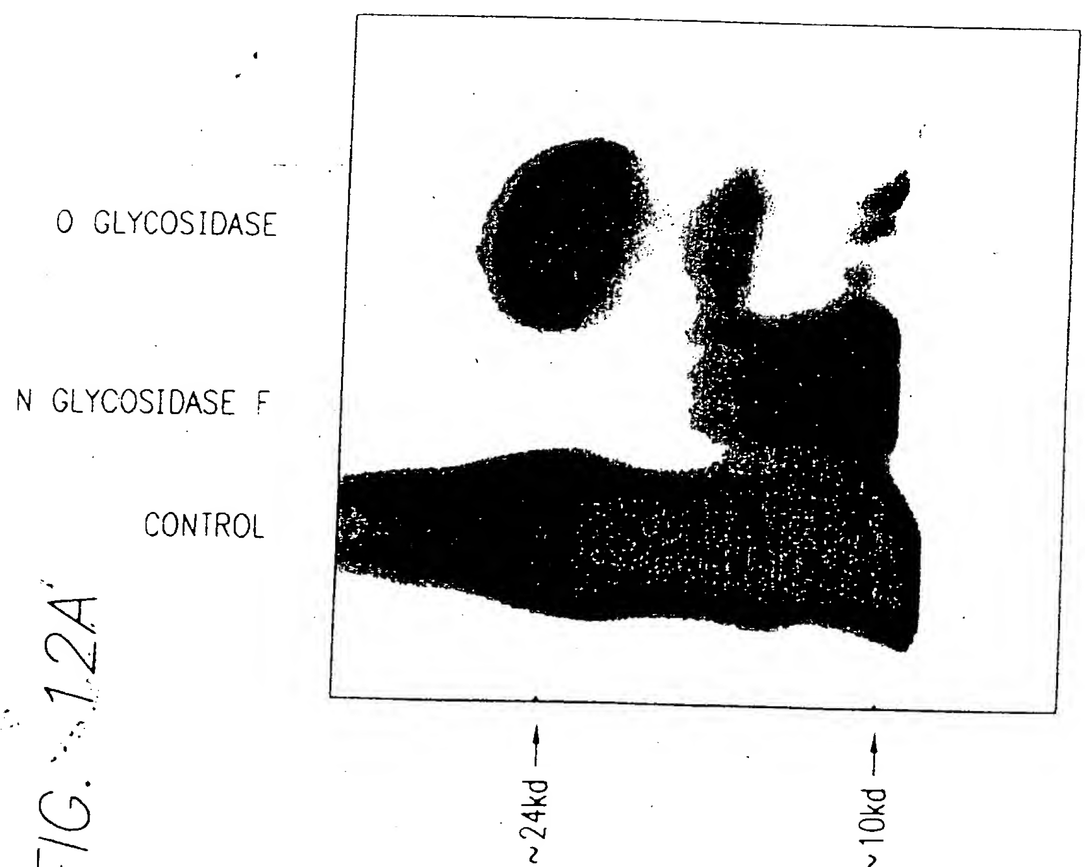


FIG. 12A

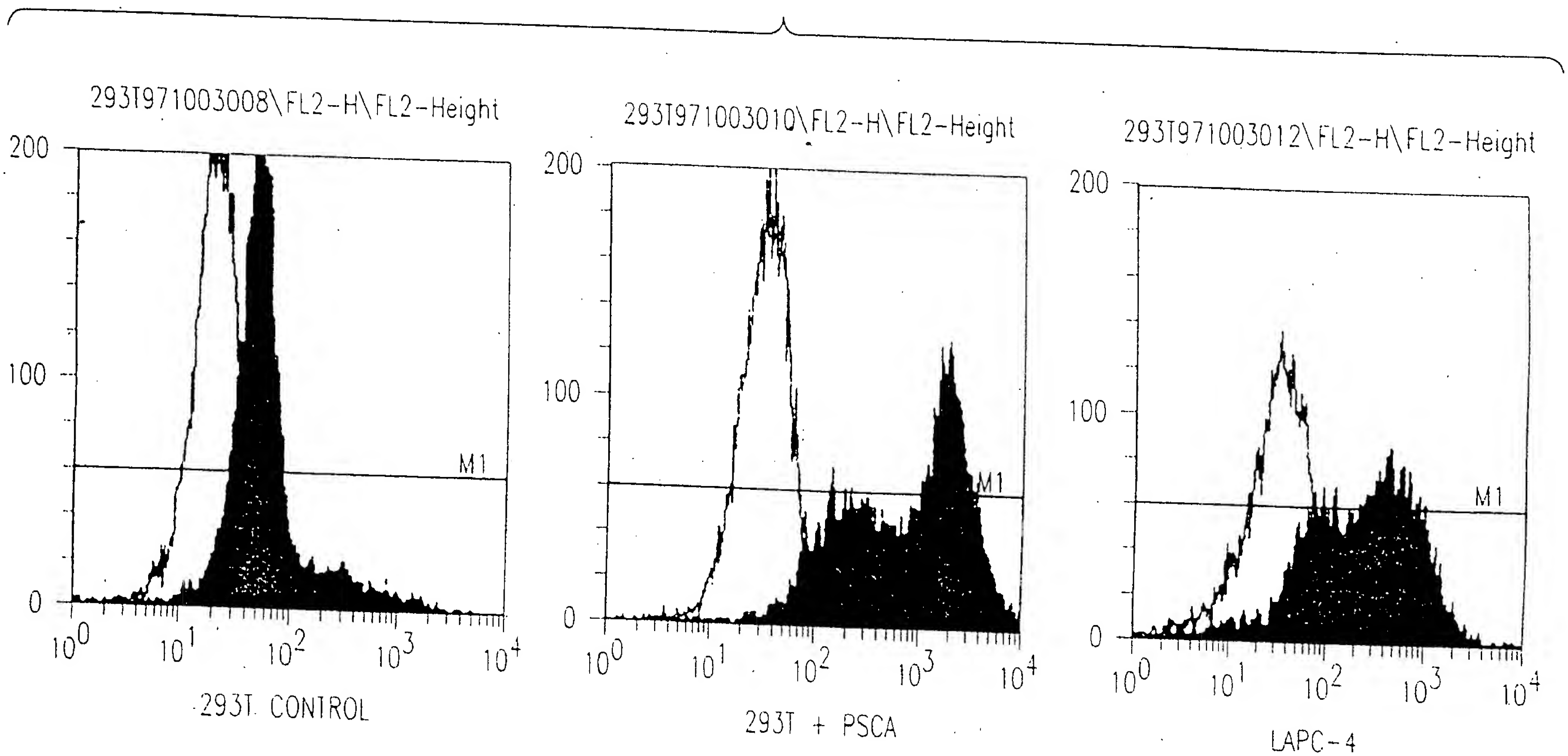

293T971003008\FL2-H\FL2-Height
200
100
0
M1
10^0 10^1 10^2 10^3 10^4
293T CONTROL
293T971003010\FL2-H\FL2-Height
200
100
0
M1
10^0 10^1 10^2 10^3 10^4
293T + PSCA
293T971003012\FL2-H\FL2-Height
200
100
0
M1
10^0 10^1 10^2 10^3 10^4
LAPC-4

FIG. 12C

FIG. 13

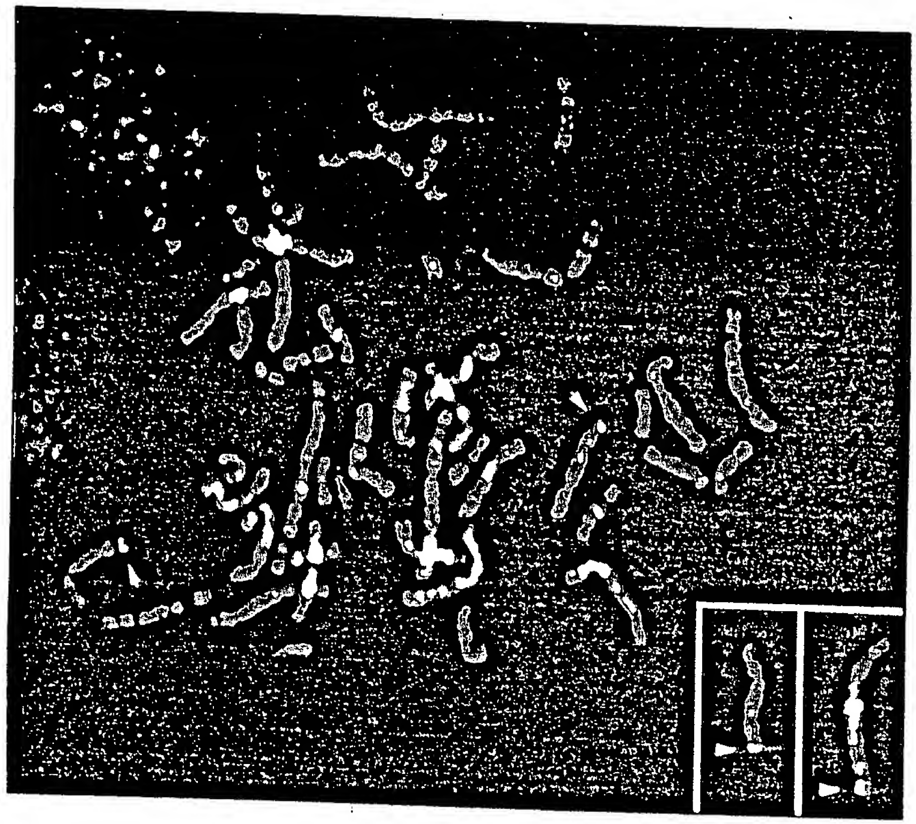


FIG. 14A

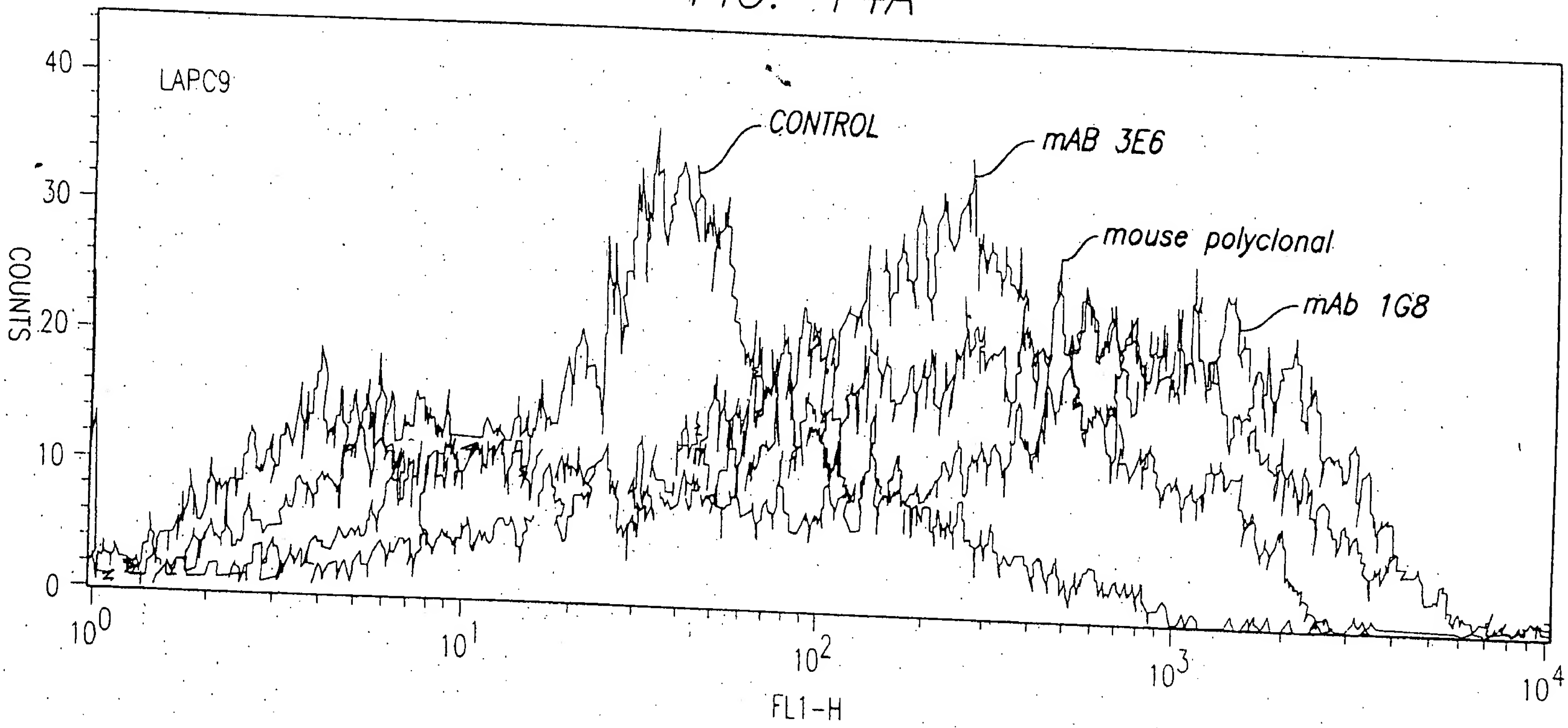
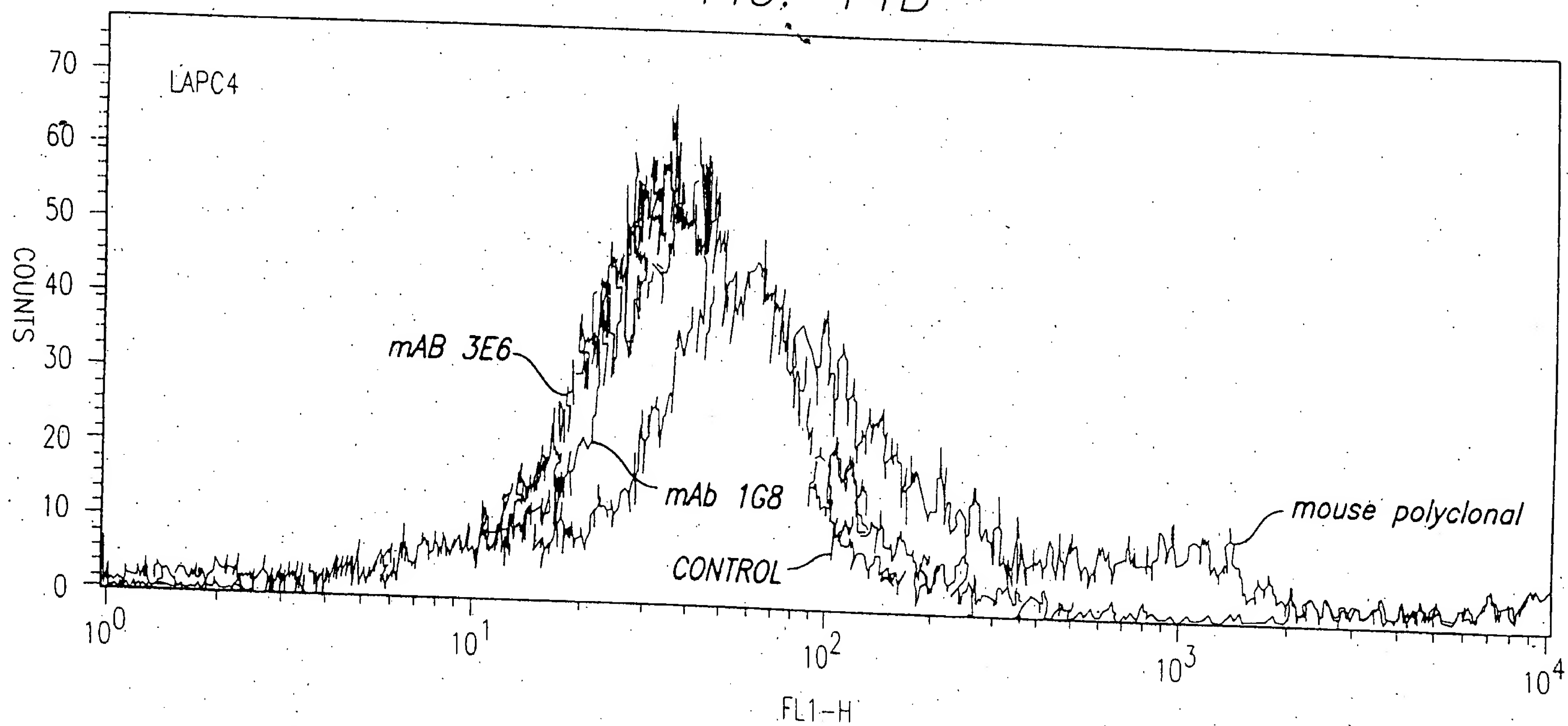
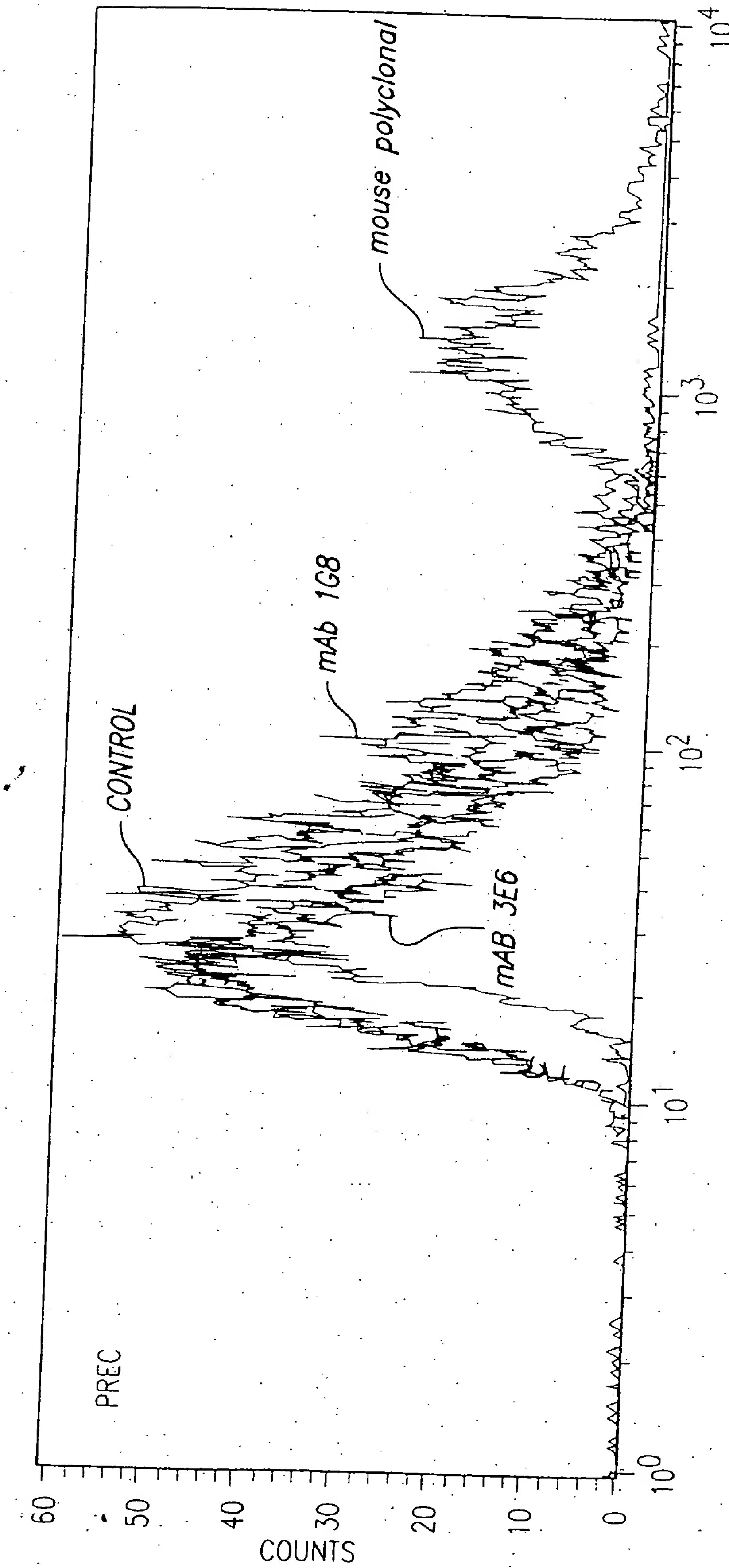

LAPC9
CONTROL
mAB 3E6
mouse polyclonal
mAb 1G8
COUNTS
0
10
20
30
40
10^0
10^1
10^2
10^3
10^4
FL1-H

FIG. 14B



LAPC4
70
60
50
40
30
20
10
0
COUNTS
mAB 3E6
mAb 1G8
CONTROL
mouse polyclonal
10^0
10^1
10^2
10^3
10^4
FL1-H

FIG. 14C



CONTROL
mAb 1G8
mouse polyclonal
mAB 3E6
PREC
COUNTS
FL1-H
60
50
40
30
20
10
0
10^0
10^1
10^2
10^3
10^4

mAb	ISOTYPE		FL (18-98)	N (2-50)	M (46-109)	C (85-123)
			EPITOPE MAP			
1G8	IgG1	k	2.039	0.007	0.628	0.000
2H9	IgG1	k	1.318	0.863	0.032	0.021
3C5	IgG2a	k	2.893	1.965	0.016	0.005
3E6	IgG3	k	0.328	0.024	0.069	0.370
4A10	IgG2a	k	2.039	1.315	0.000	0.014
2A2	IgG2a	k	1.366	0.733	0.010	0.003
3G3	IgG2a	k	2.805	1.731	0.004	0.000

FIG. 15A

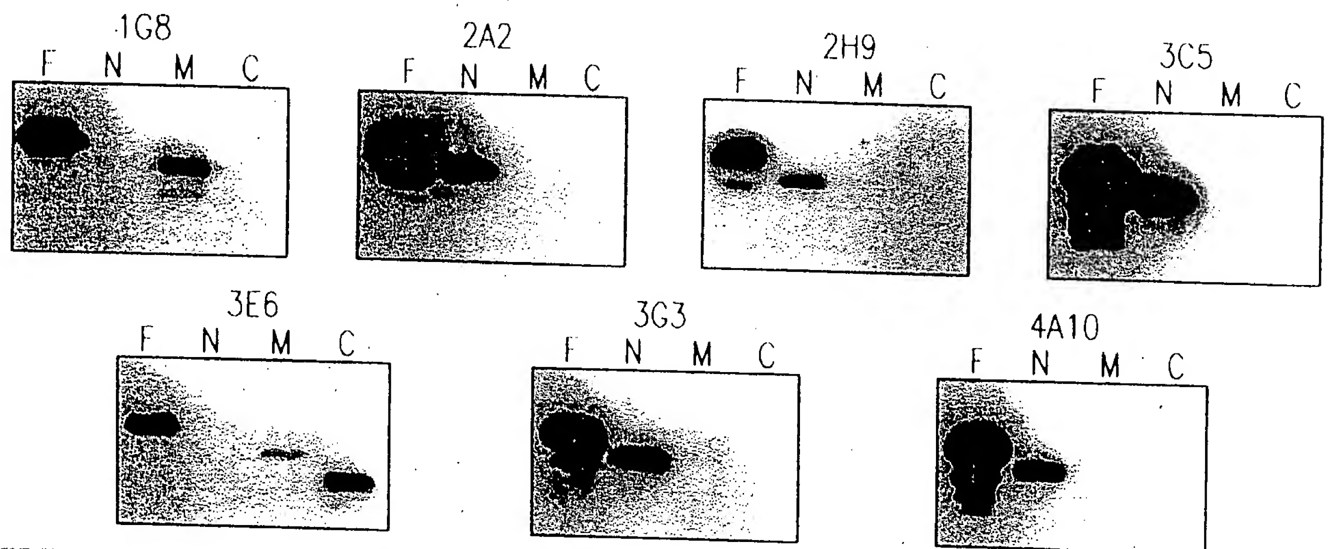


FIG. 15B

PROSTATE STEM CELL ANTIGEN (PSCA) IS A GPI-ANCHORED PROTEIN

```
1    M K I F L P V L L A A L L G V E R A S S     hSCA-2
1    M K A V L L A L L M A G L A L Q P G T A     hPSCA
1    M K T V L F L L L A T Y L A L H P G A A     mPSCA

21   L M C F S C L N Q K S N* L Y C L K P T I
21   L L C Y S C K A Q V S N* E D C L Q V E N*
21   L Q C Y S C T A Q M N N* R D C L N V Q N*

41   C S D Q D N Y C V T V S A S A G I G N L
41   C T Q L G E Q C W T A R I R A V G L L T
41   C S L D Q H S C F I S R I R A I G L V T

61   V T F G H S L S K T C S P A C P I P E G
61   V - - - - - - I S K G C S L N C V D D S Q
61   V - - - - - - I S K G C S S Q C E D D S E

81   V N V G V A S M G I S C C Q S F L C N* F
76   D Y Y V G K K - N* I T C C D T D L C N* A
76   N Y Y L G K K - N* I T C C Y S D L C N* V

101  S A A D G G L R A S V T L L G A G L L L
95   S G A H A L Q P A A A I L A L L P A L G
95   N G A H T L K P P T T L G L L T V L C S

121  S L L P A L L R F G P
115  L L L W G P G Q L - -
115  L L L W G S S R L - -
```

FIG. 16A

PROSTATE STEM CELL ANTIGEN (PSCA) IS A GPI-ANCHORED PROTEIN

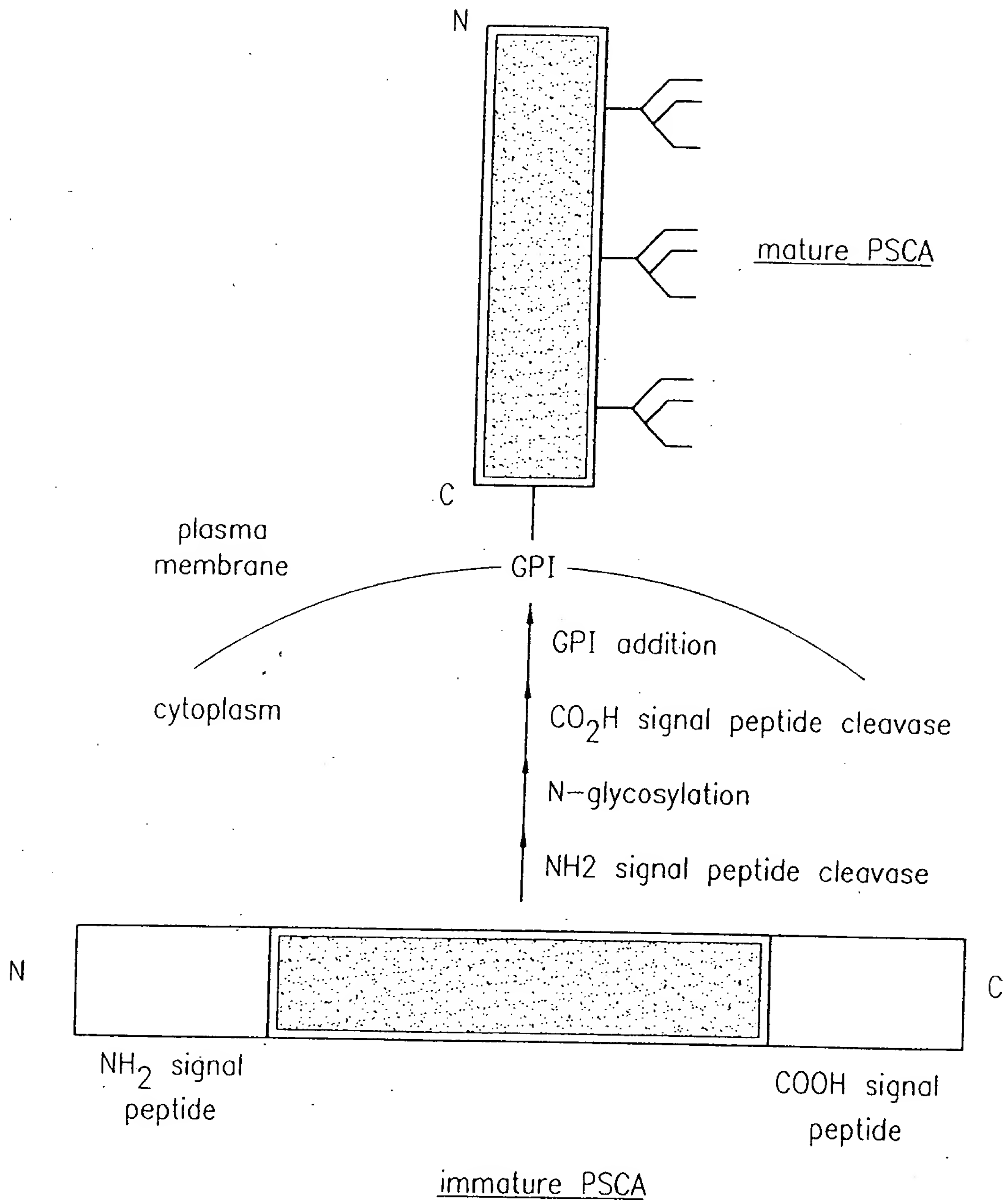


FIG. 16B

FIG. 17

FISH ANALYSIS OF PSCA AND c-myc IN PROSTATE CANCER

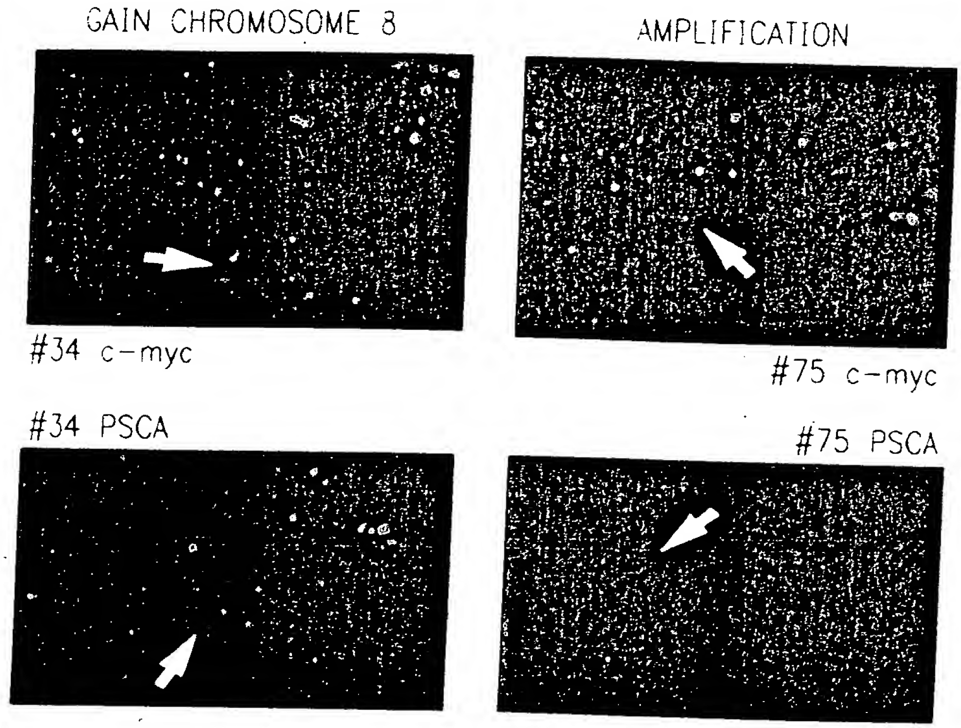
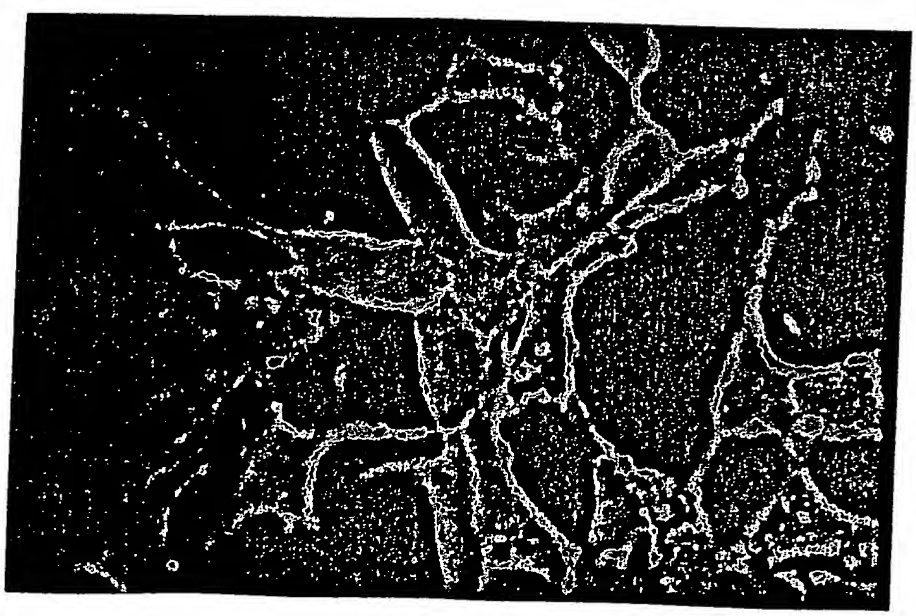


FIG. 18



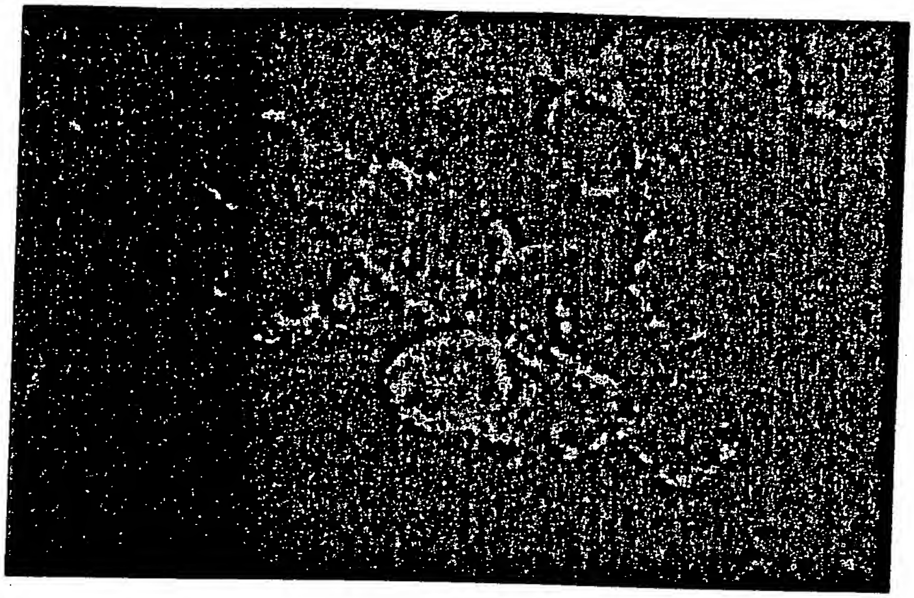


FIG. 19

FIG. 20

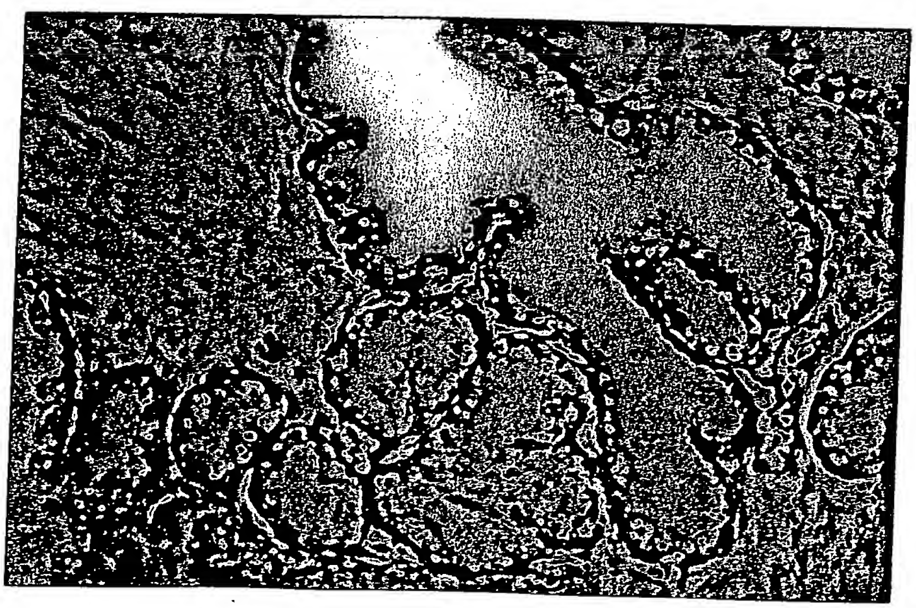


FIG. 21

PSCA IMMUNOSTAINING OF PRIMARY TUMORS

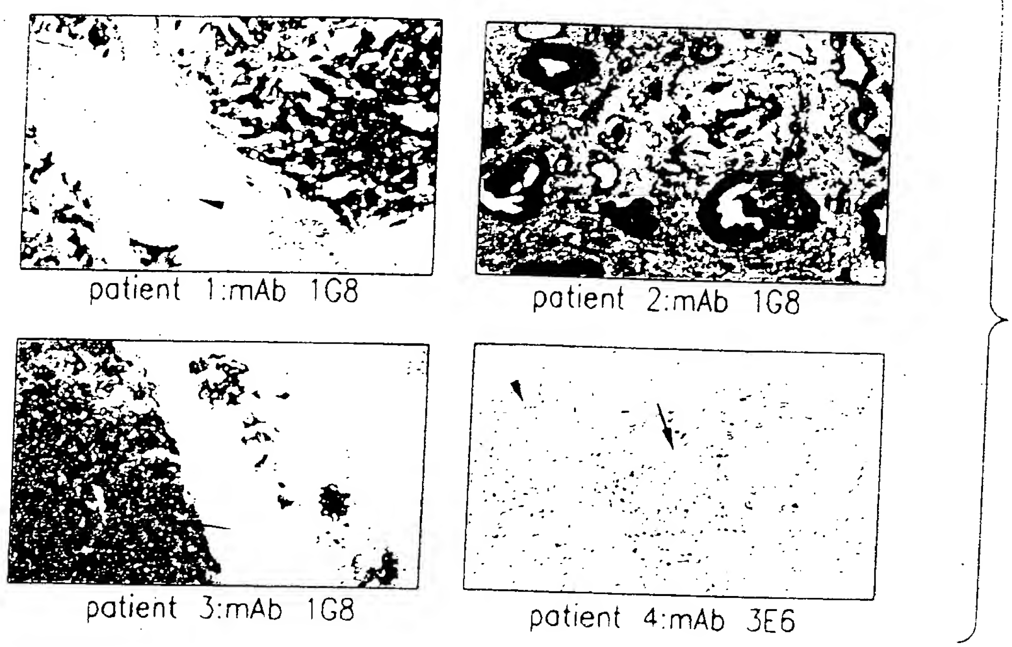


FIG. 22

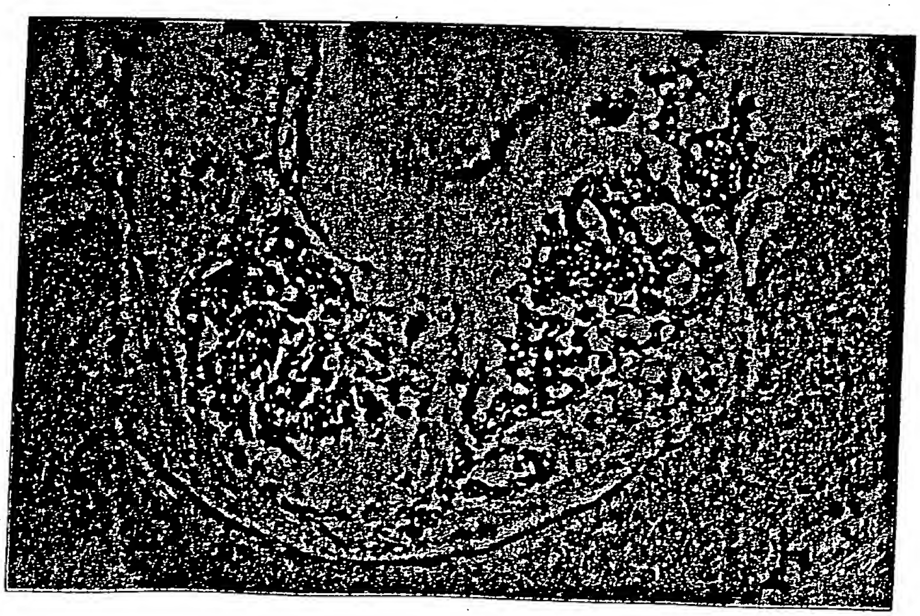
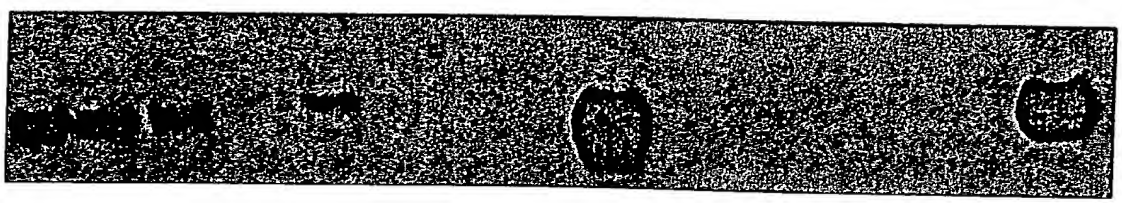


FIG. 23

FIG. 24

FIG. 25



PSCA NORTHERN

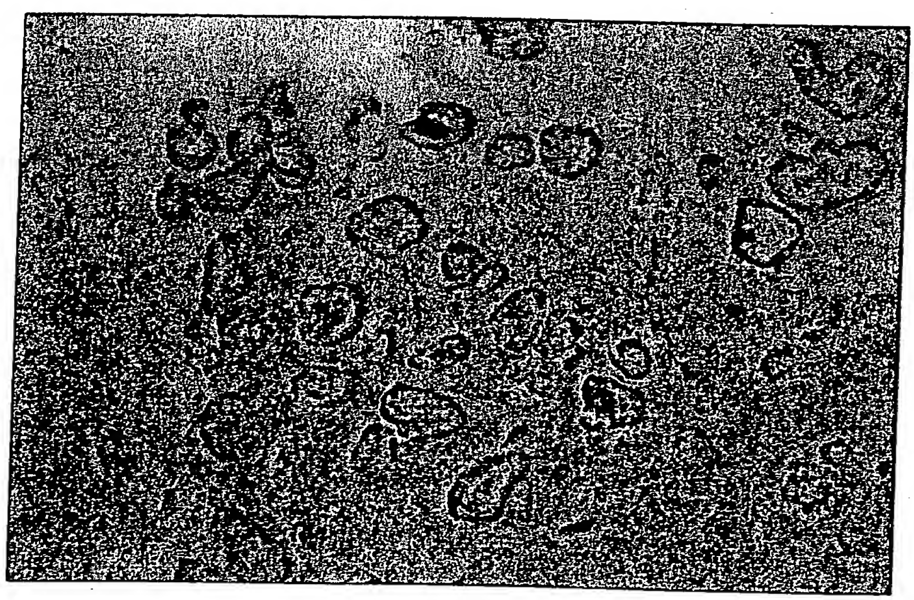


FIG. 26

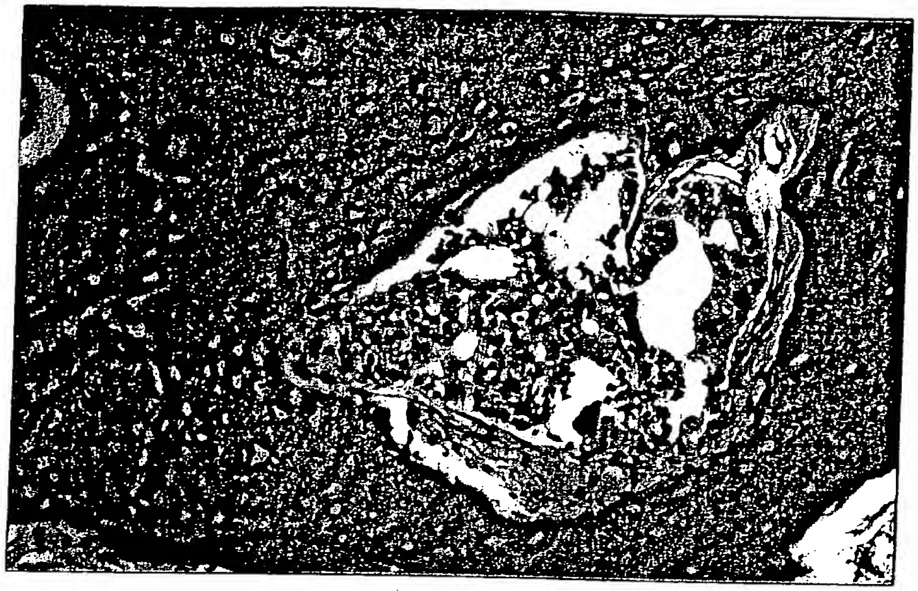
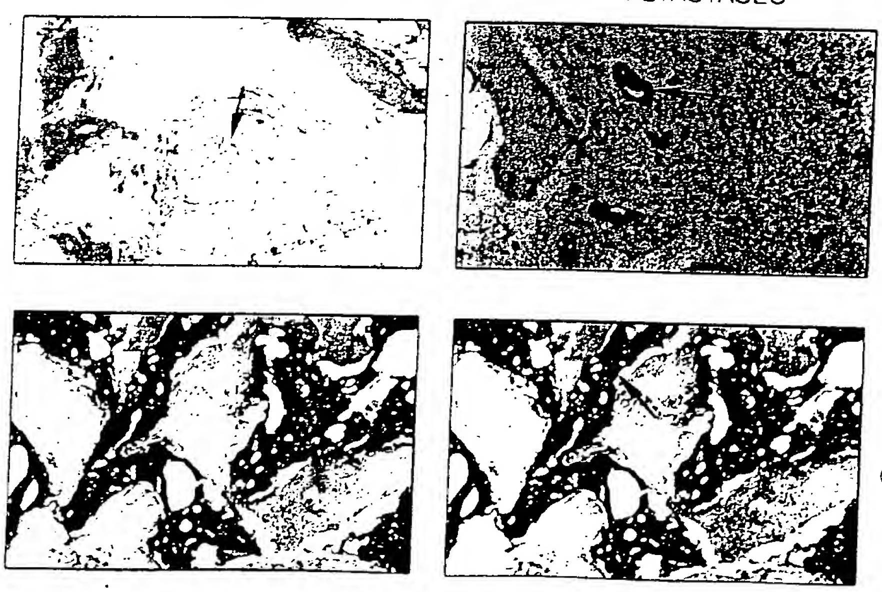


FIG. 27

PSCA IMMUNOSTAINING OF BONY METASTASES



Patient 5: H and E and mAb 1G8

Patient 4: H and E and mAb 3E6

FIG. 28

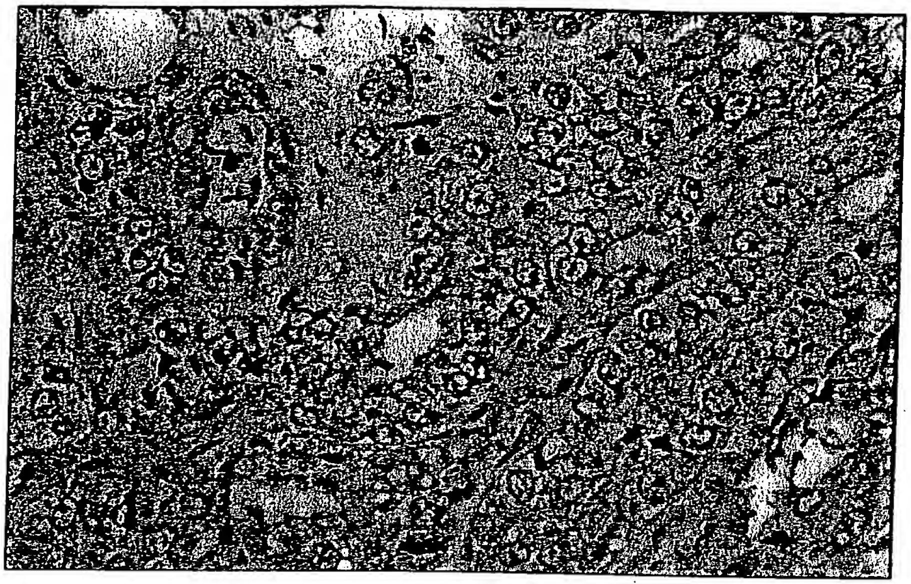


FIG. 29

FIG. 30

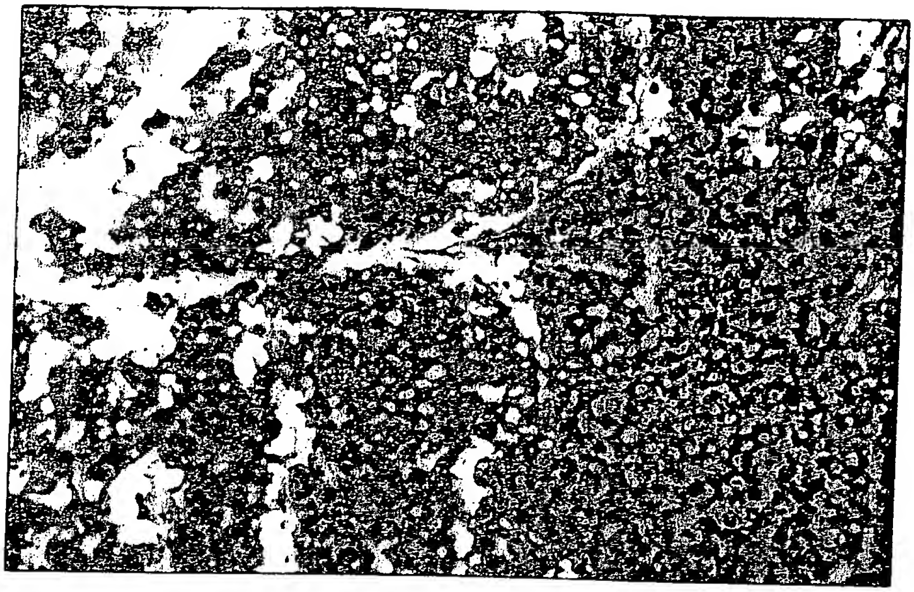


FIG. 31

FIG. 32

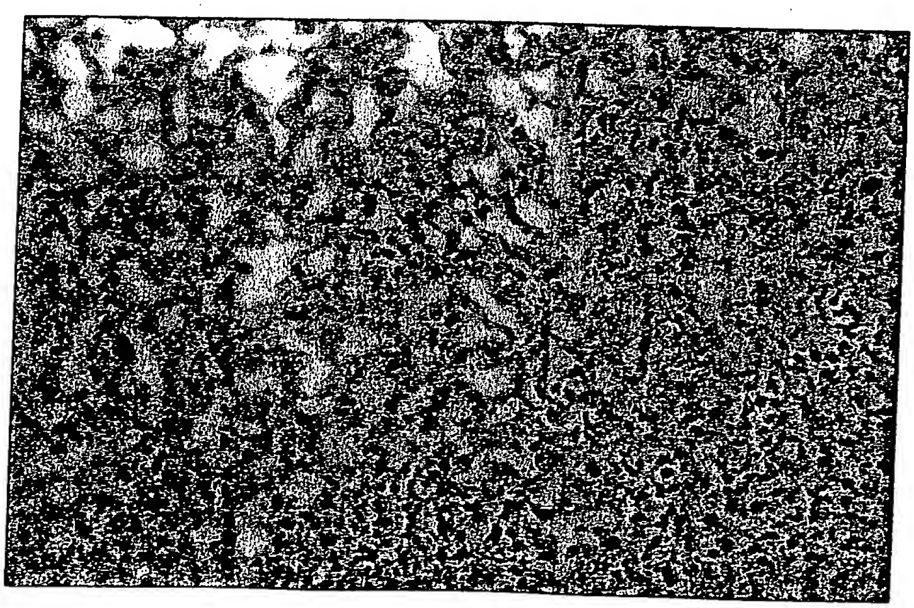
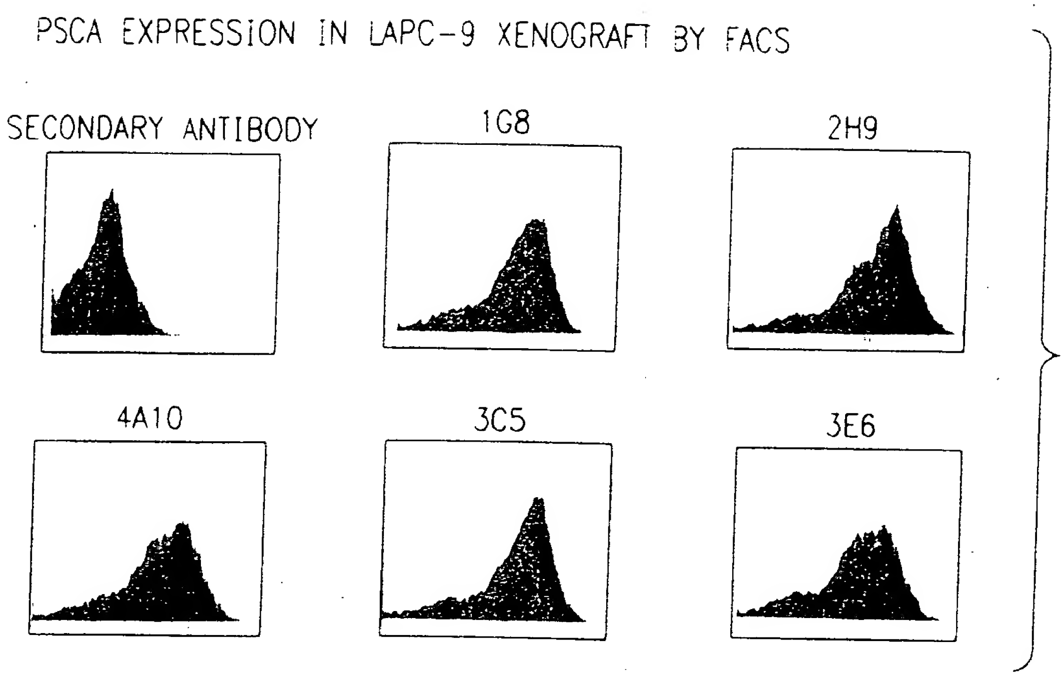


FIG. 33


PSCA EXPRESSION IN LAPC-9 XENOGRAFT BY FACS
SECONDARY ANTIBODY
1G8
2H9
4A10
3C5
3E6

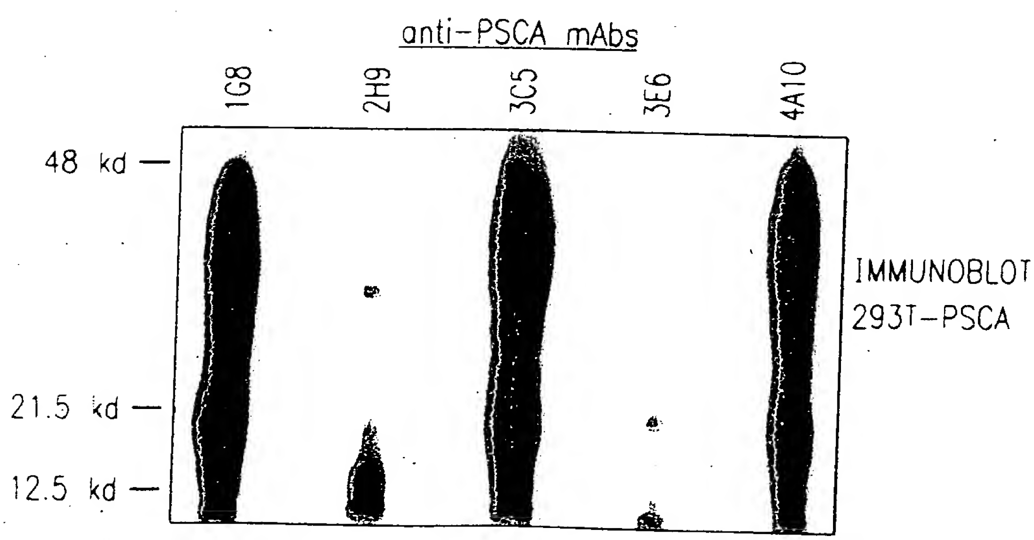
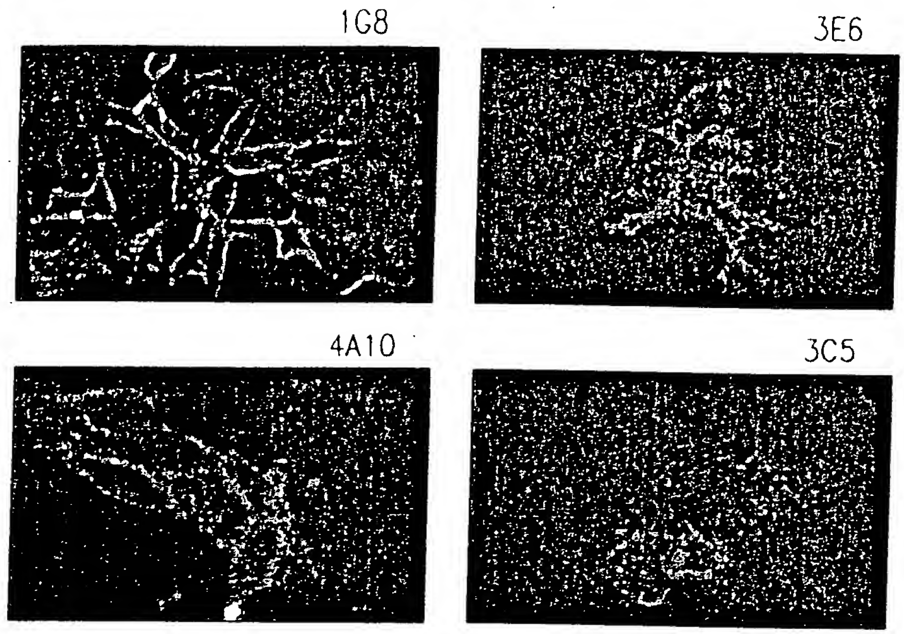

anti-PSCA mAbs
1G8
2H9
3C5
3E6
4A10
48 kd
21.5 kd
12.5 kd
IMMUNOBLOT:
293T-PSCA

FIG. 34

FIG. 35

IMMUNOFLUORESCENT STAINING OF LNCaP-PSCA CELLS



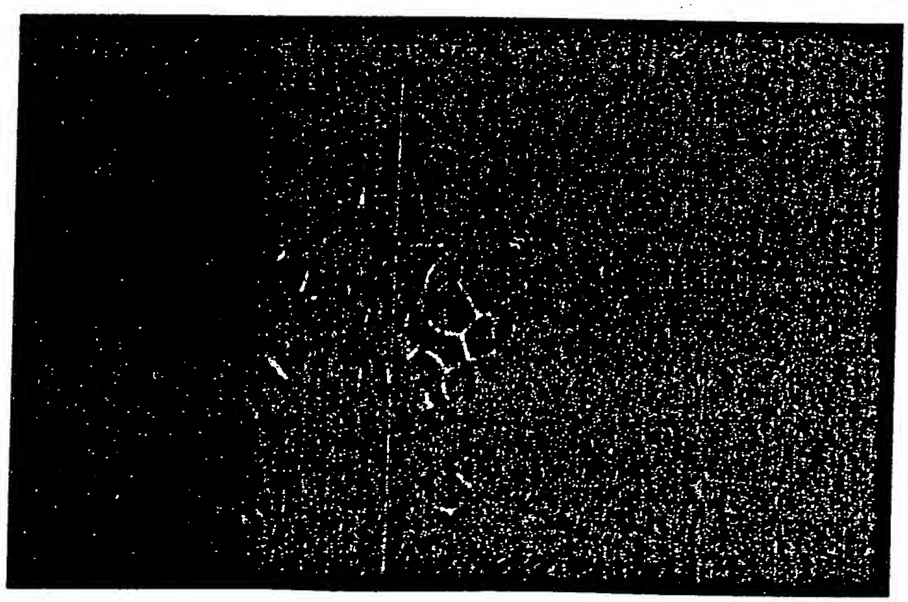


FIG. 36

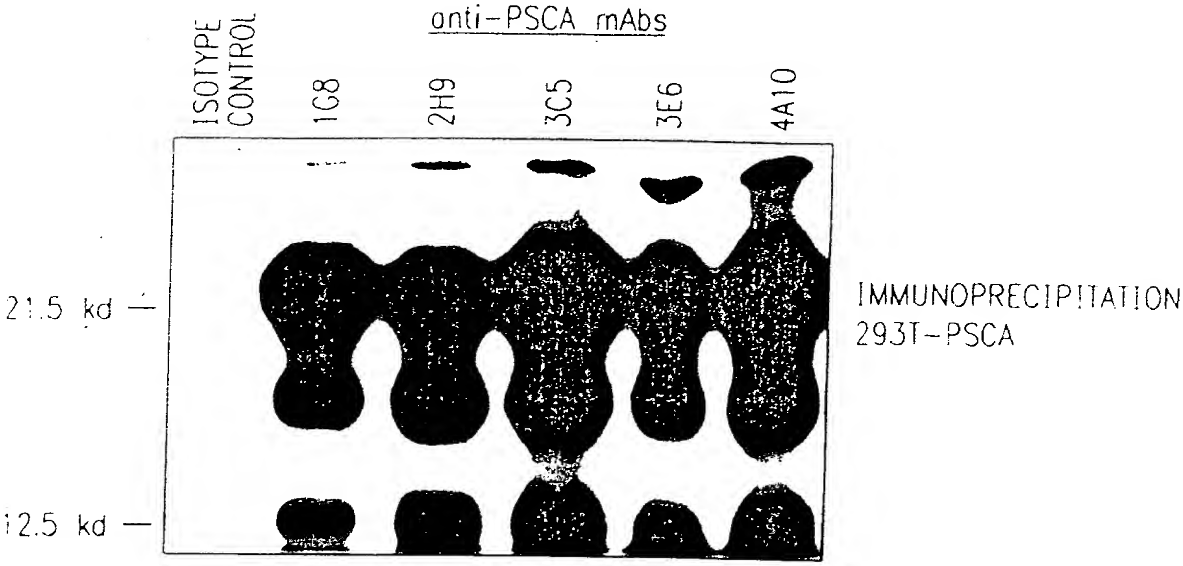

anti-PSCA mAbs
ISOTYPE CONTROL
1G8
2H9
3C5
3E6
4A10
21.5 kd
12.5 kd
IMMUNOPRECIPITATION: 293T-PSCA

FIG. 37

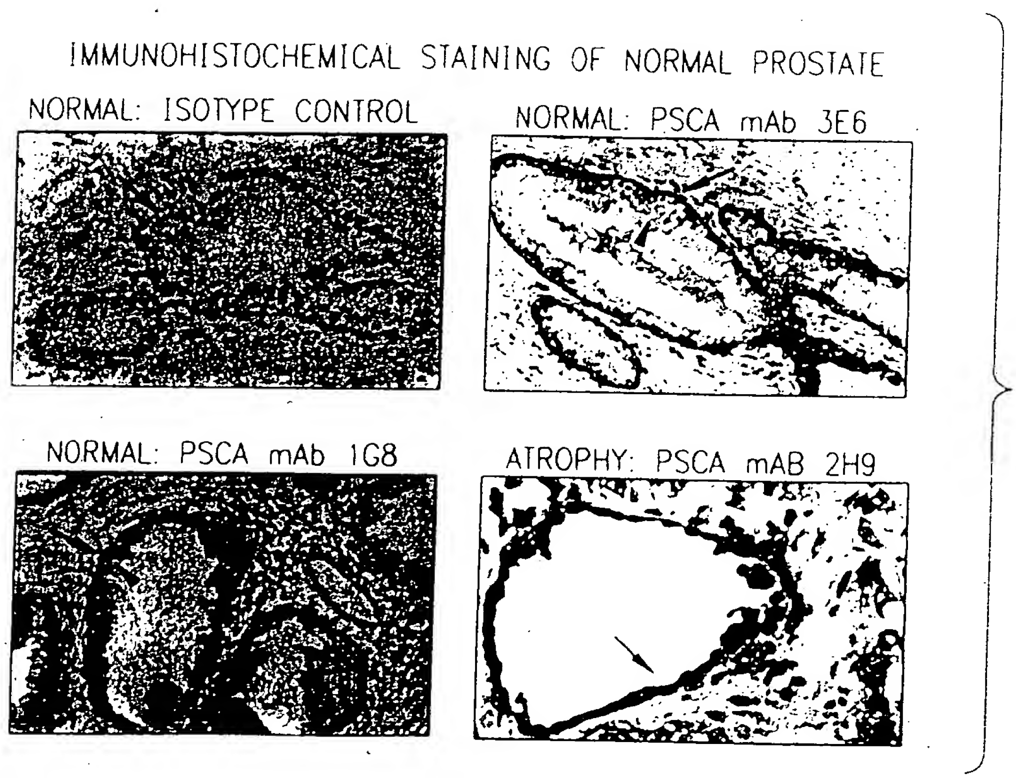
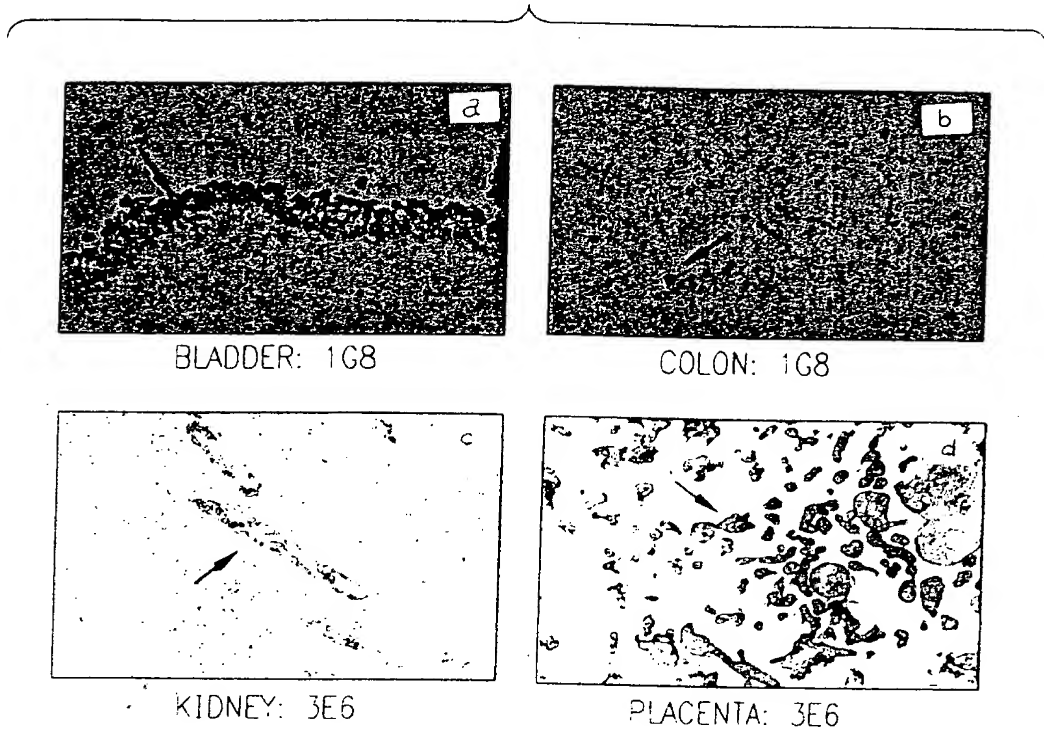

IMMUNOHISTOCHEMICAL STAINING OF NORMAL PROSTATE
NORMAL: ISOTYPE CONTROL
NORMAL: PSCA mAb 3E6
NORMAL: PSCA mAb 1G8
ATROPHY: PSCA mAB 2H9

FIG. 38

FIG. 39A



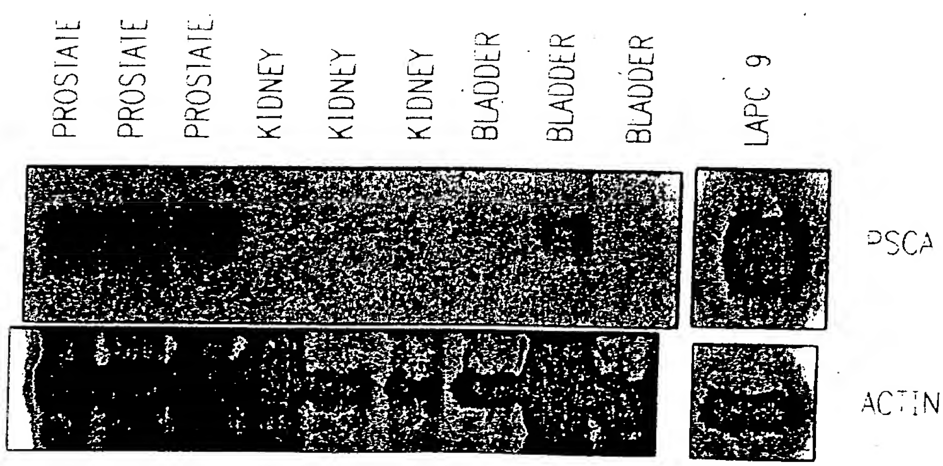


FIG. 39B

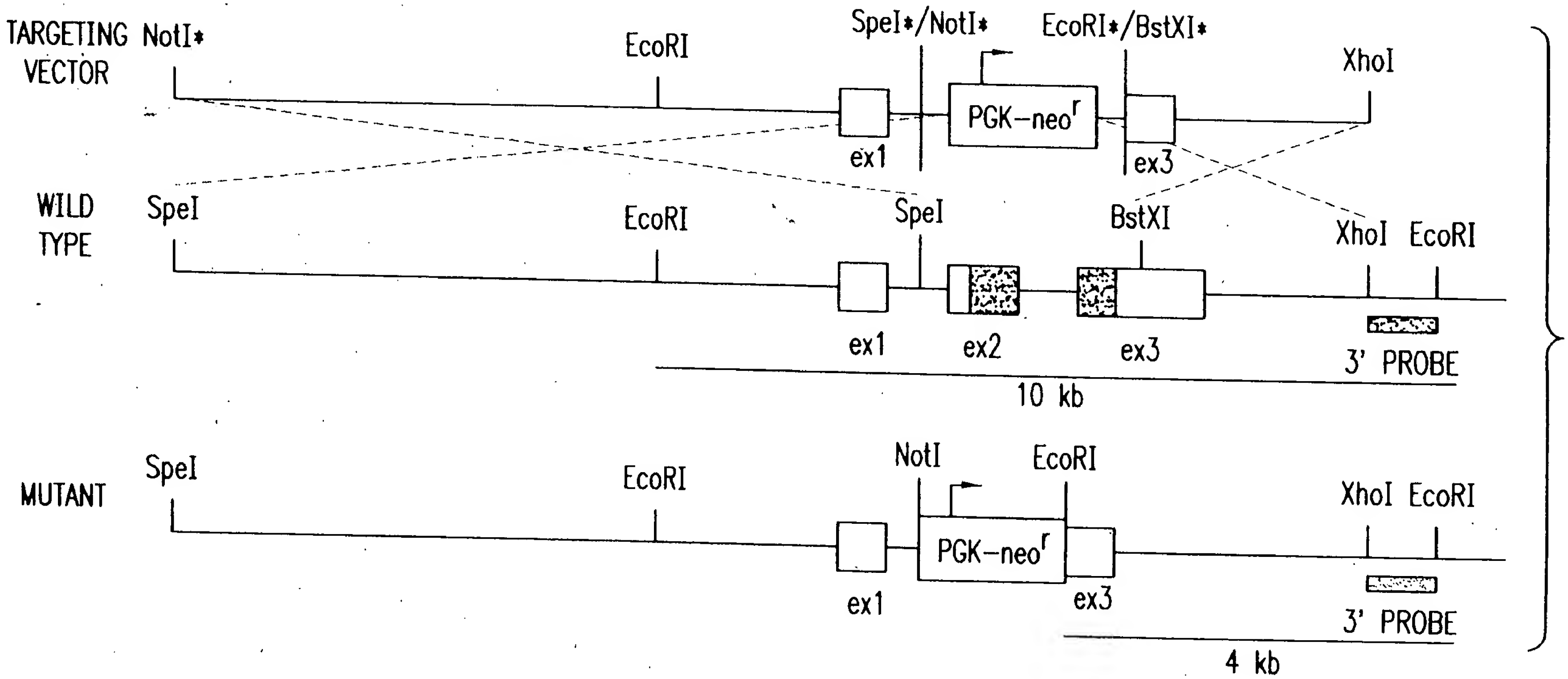


FIG. 40A

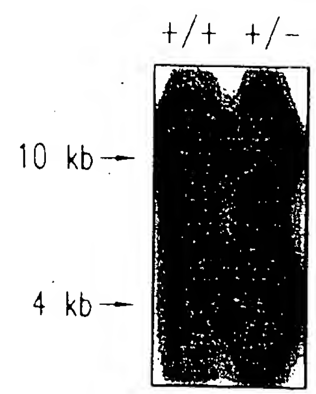
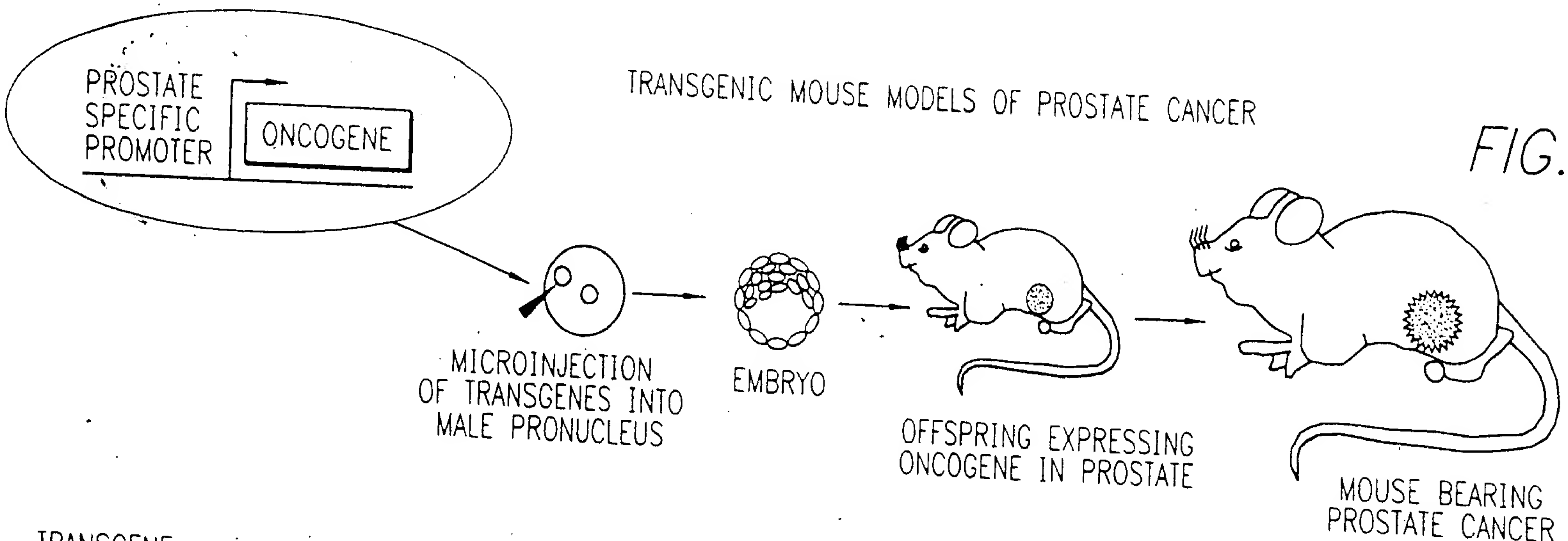


FIG. 40B

TRANSGENIC MOUSE MODELS OF PROSTATE CANCER

FIG. 41



TRANSGENE	TARGET TISSUES	CHARACTERISTICS
C3(1) (−3 kb)/ SV40 LARGE+SMALL, T MAROULAKOU et al. 1994 PNAS	PROSTATE (SECRETORY CELLS) URETHRAL, MAMMARY AND SWEAT GLAND	LOW-GRADE PIN 8–12 WKS HIGH-GRADE PIN 8–12 WKS INVASIVE CARCICINOMA 28 WKS NO METASTASES
PROBASIN (−426 bp)/ SV40 LARGE+SMALL, T GREENBERG et al. 1995 PNAS	PROSTATE (SECRETORY CELLS)	LOW-GRADE PIN 5–8 WKS HIGH-GRADE PIN 8–12 WKS INVASIVE CARCICINOMA 12 WKS METASTASES IN LYMPH NODE, LUNG, LIVER AND BONE
CRYPTDIN2 (−6.5 kb)/ SV40 LARGE+SMALL, T GARABEDIAN et al. 1998 PNAS	PROSTATE (NEUROENDOCRINE CELLS) SMALL INTESTINE	LOW-GRADE PIN 8–12 WKS HIGH-GRADE PIN 8–12 WKS INVASIVE CARCICINOMA 16 WKS METASTASES IN LYMPH NODE, LUNG, LIVER, AND BONE

REPORTER GENE CONSTRUCTS FOR TRANSFECTION ASSAY

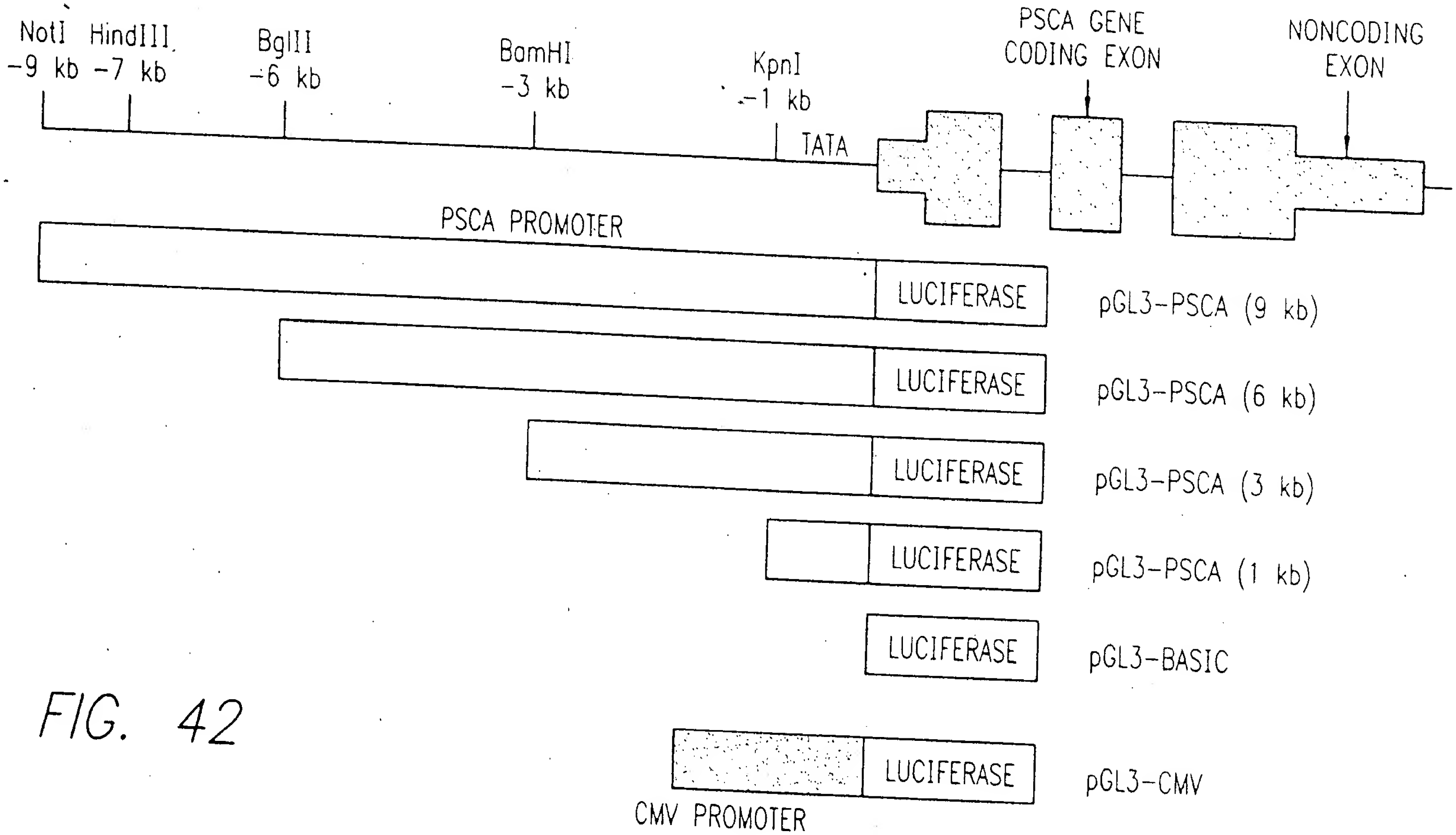


FIG. 42

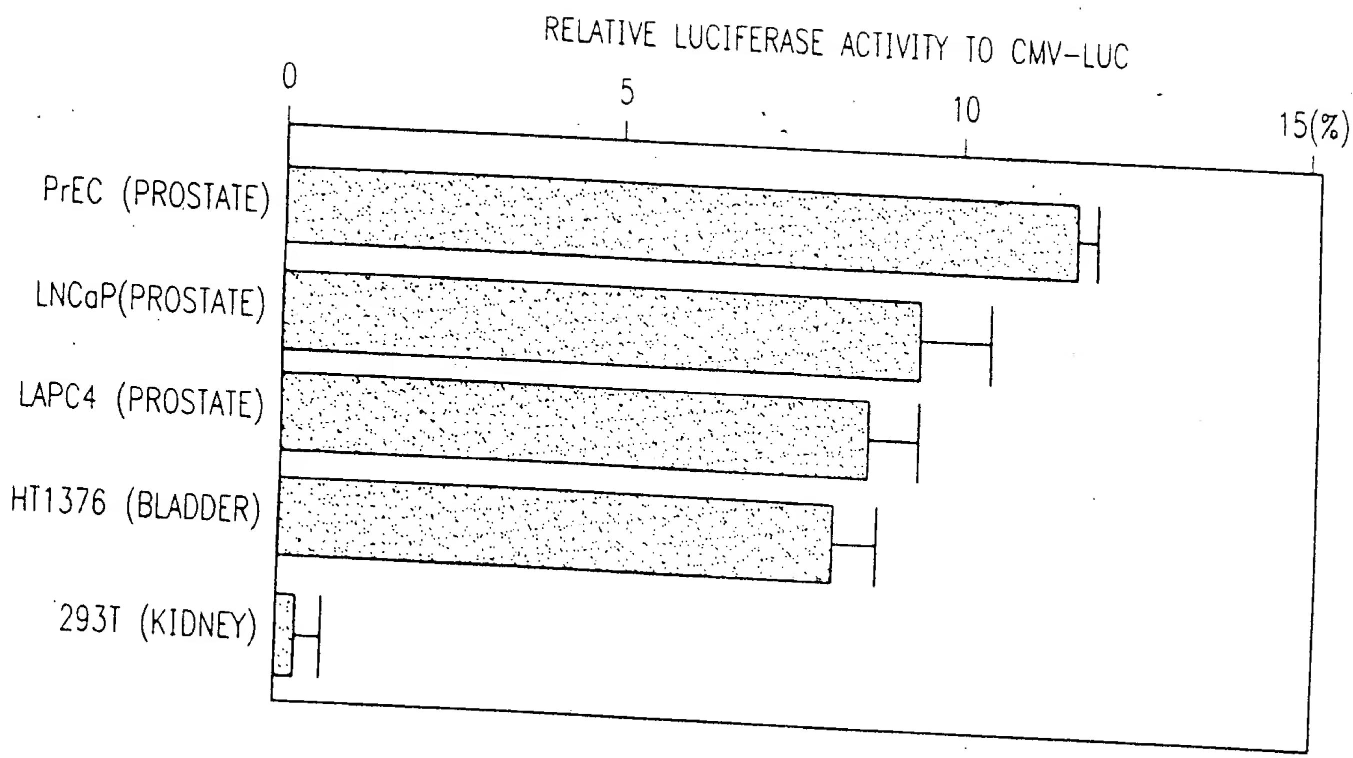

RELATIVE LUCIFERASE ACTIVITY TO CMV-LUC
0
5
10
15(%)
PrEC (PROSTATE)
LNCaP(PROSTATE)
LAPC4 (PROSTATE)
HT1376 (BLADDER)
293T (KIDNEY)

FIG. 43

IDENTIFICATION OF PROSTATE-SPECIFIC ELEMENTS WITHIN PSCA PROMOTER SEQUENCES

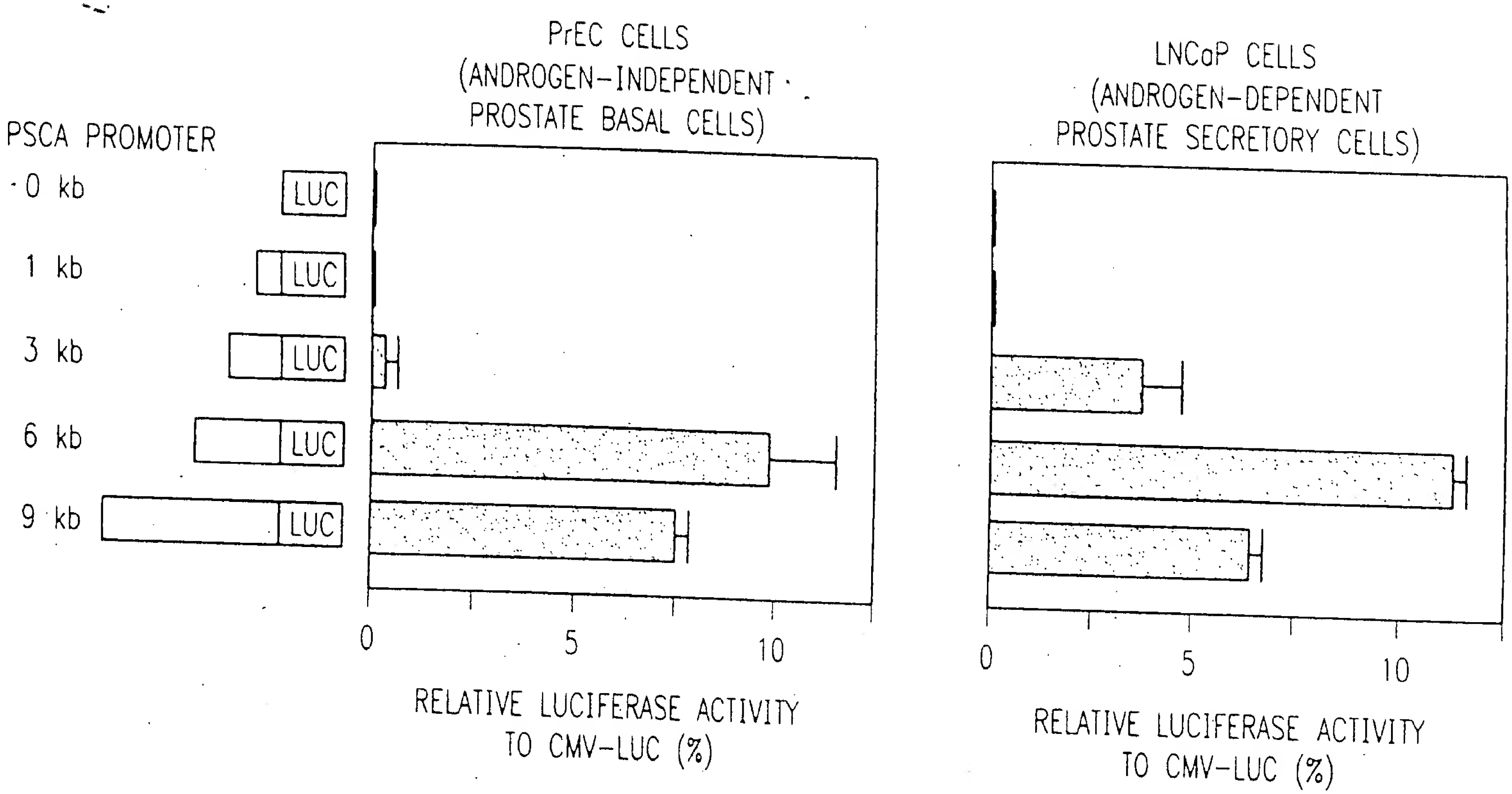
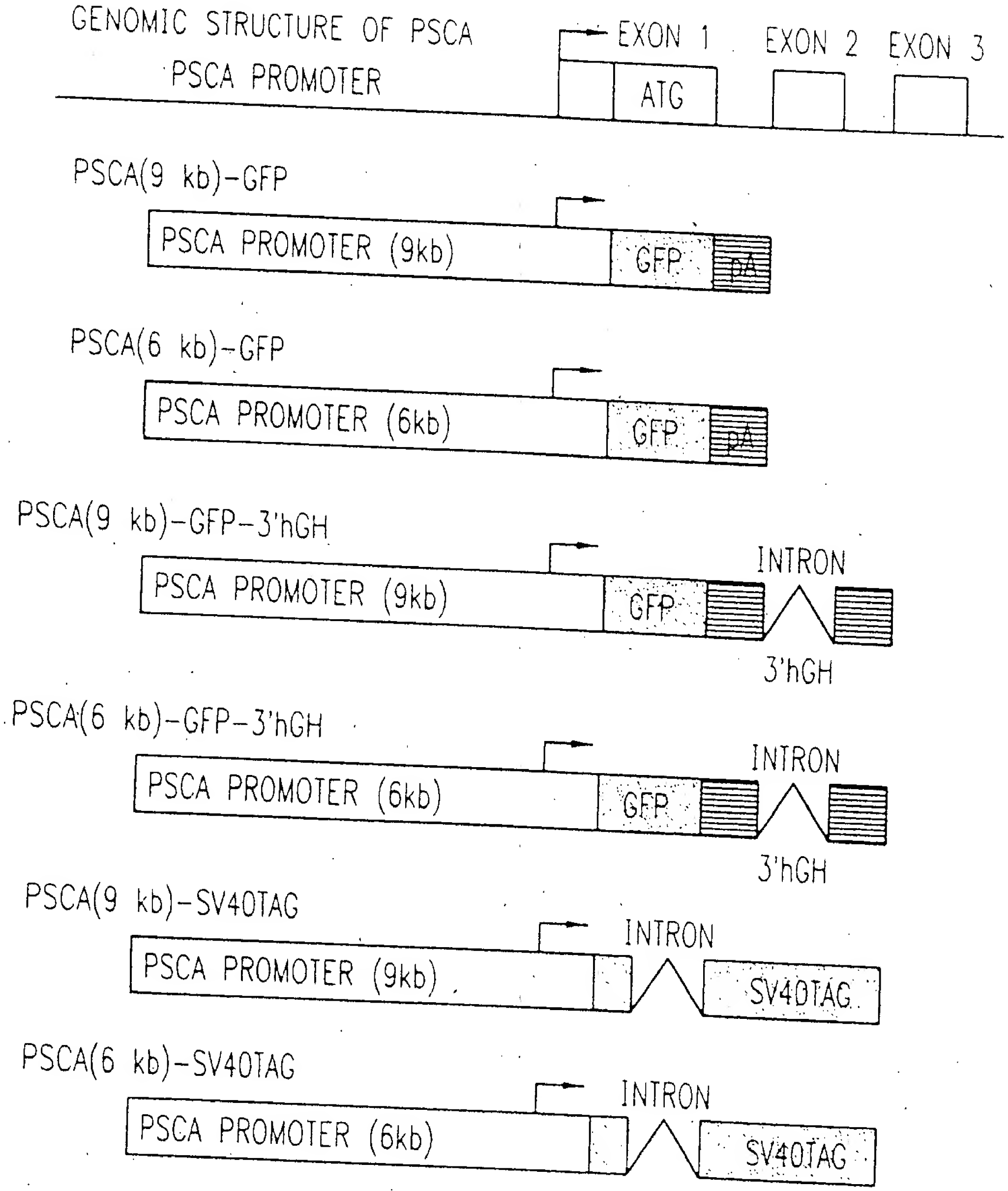


FIG. 44

FIG. 45

UPDATE OF TRANSGENIC MOUSE PROJECTS



NUMBER OF FOUNDERS (DNA POSITIVE)
2
1
6
8
3
9

NEGATIVE TISSUES
STOMACH
SMALL INTESTINE
COLON
SEMINAL VESICLE
URETHRA
TESTIS
LIVER
KIDNEY
LUNG
BRAIN
HEART
SKELETAL MUSCLE
OVARY
UTERUS

WHOLE-MOUNT GREEN FLUORECENCE IMAGE

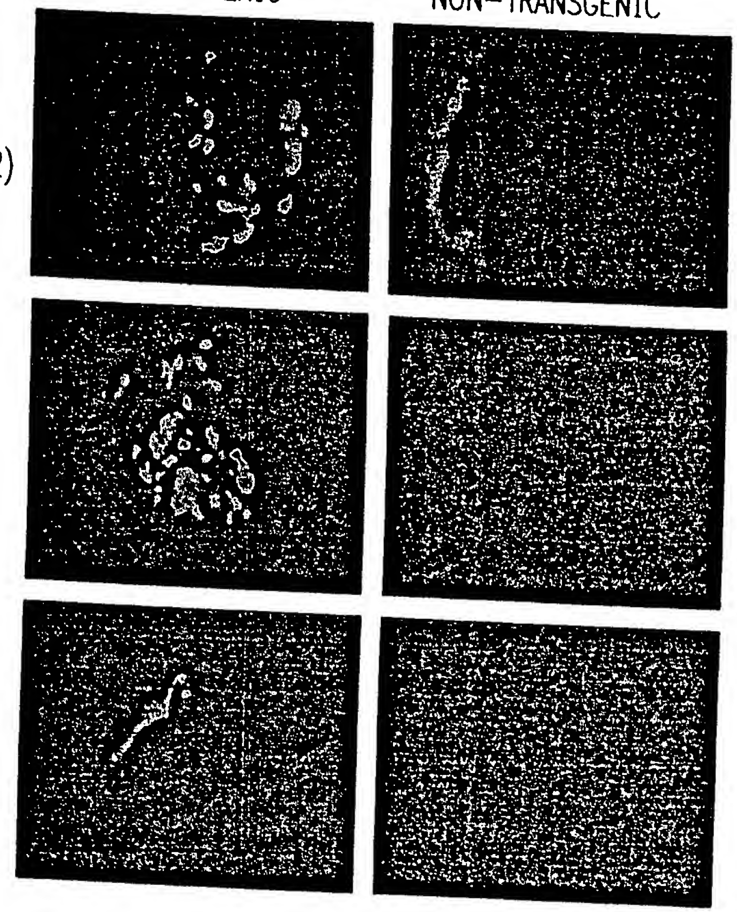
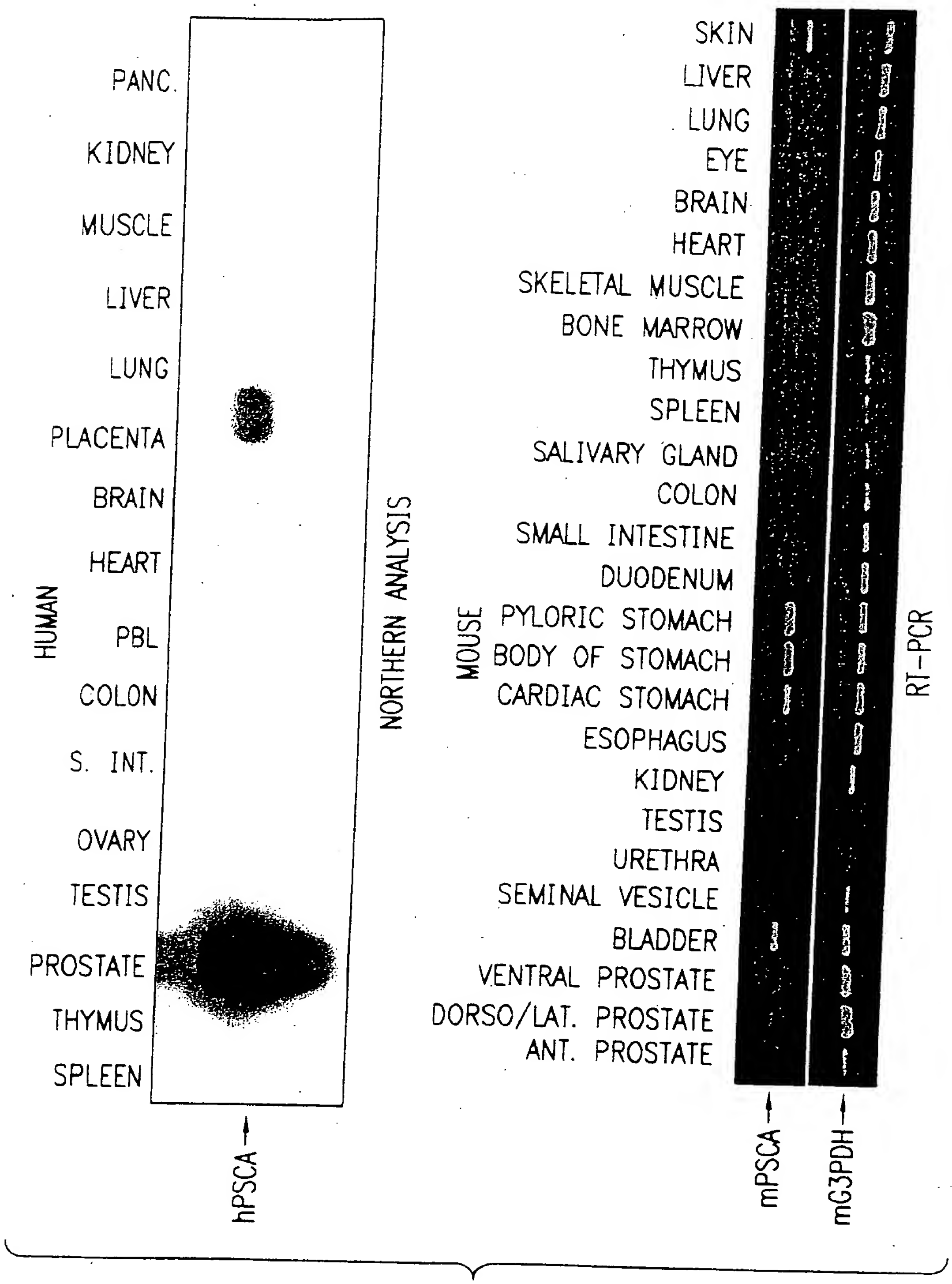


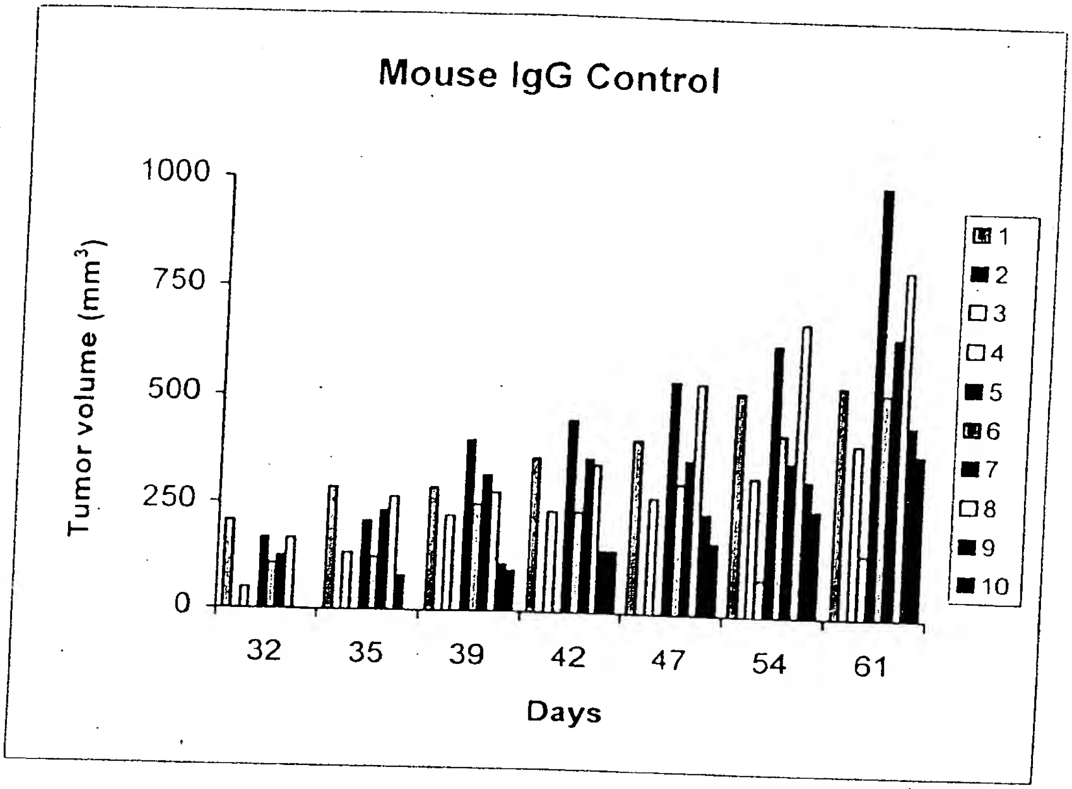
FIG. 46



HUMAN
PANC.
KIDNEY
MUSCLE
LIVER
LUNG
PLACENTA
BRAIN
HEART
PBL
COLON
S. INT.
OVARY
TESTIS
PROSTATE
THYMUS
SPLEEN
hPSCA
NORTHERN ANALYSIS
MOUSE
SKIN
LIVER
LUNG
EYE
BRAIN
HEART
SKELETAL MUSCLE
BONE MARROW
THYMUS
SPLEEN
SALIVARY GLAND
COLON
SMALL INTESTINE
DUODENUM
PYLORIC STOMACH
BODY OF STOMACH
CARDIAC STOMACH
ESOPHAGUS
KIDNEY
TESTIS
URETHRA
SEMINAL VESICLE
BLADDER
VENTRAL PROSTATE
DORSO/LAT. PROSTATE
ANT. PROSTATE
mPSCA
mG3PDH
RT-PCR

FIG. 47

FIG. 48


Mouse IgG Control
Tumor volume (mm³)
1000
750
500
250
0
32
35
39
42
47
54
61
Days
1
2
3
4
5
6
7
8
9
10

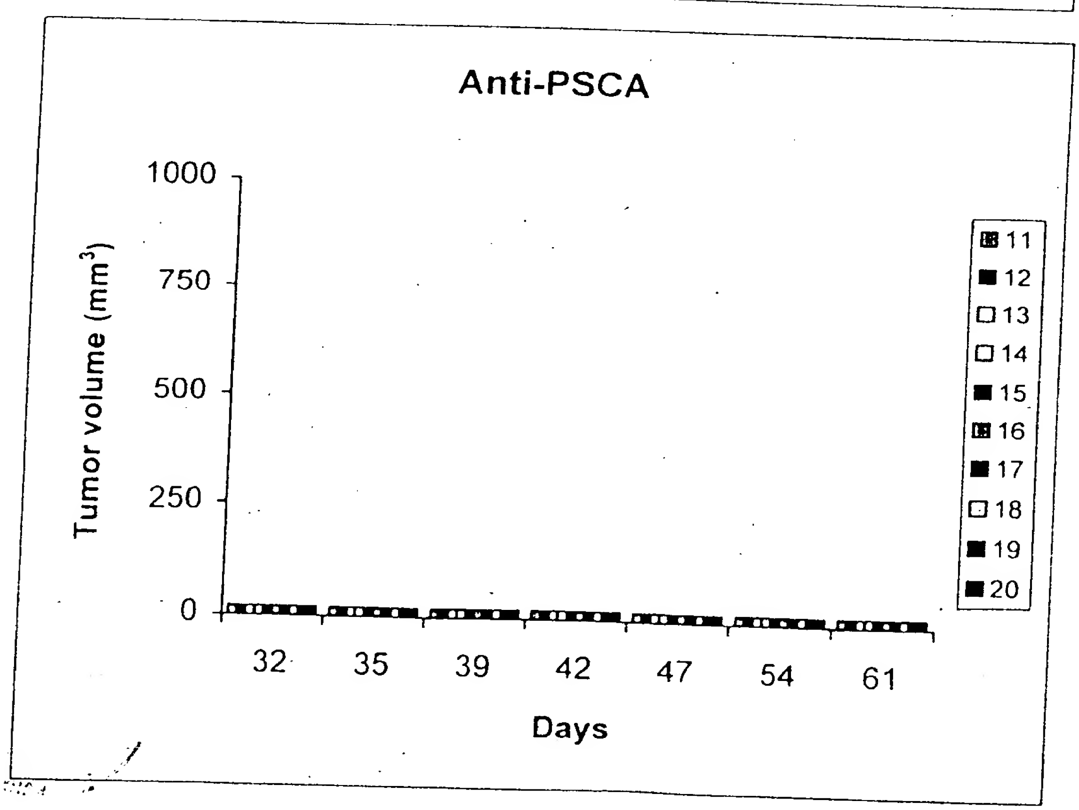

Anti-PSCA
Tumor volume (mm³)
1000
750
500
250
0
32
35
39
42
47
54
61
Days
11
12
13
14
15
16
17
18
19
20

FIG. 49

A

mAb	Isotype		Epitope recognized (OD 450 nm) F (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1	k	**1.485**	0.004	**1.273**	0.003
2A2	IgG2a	k	**0.973**	**0.631**	0.023	0.010
2H9	IgG1	k	**1.069**	**1.026**	0.002	0.001
3C5	IgG2a	k	**1.916**	**1.709**	0.006	0.002
3E6	IgG3	k	**1.609**	0.036	**1.133**	**2.118**
3G3	IgG2a	k	**2.805**	**1.731**	0.004	0.000
4A10	IgG2a	k	**1.053**	**0.493**	0.000	0.001

B

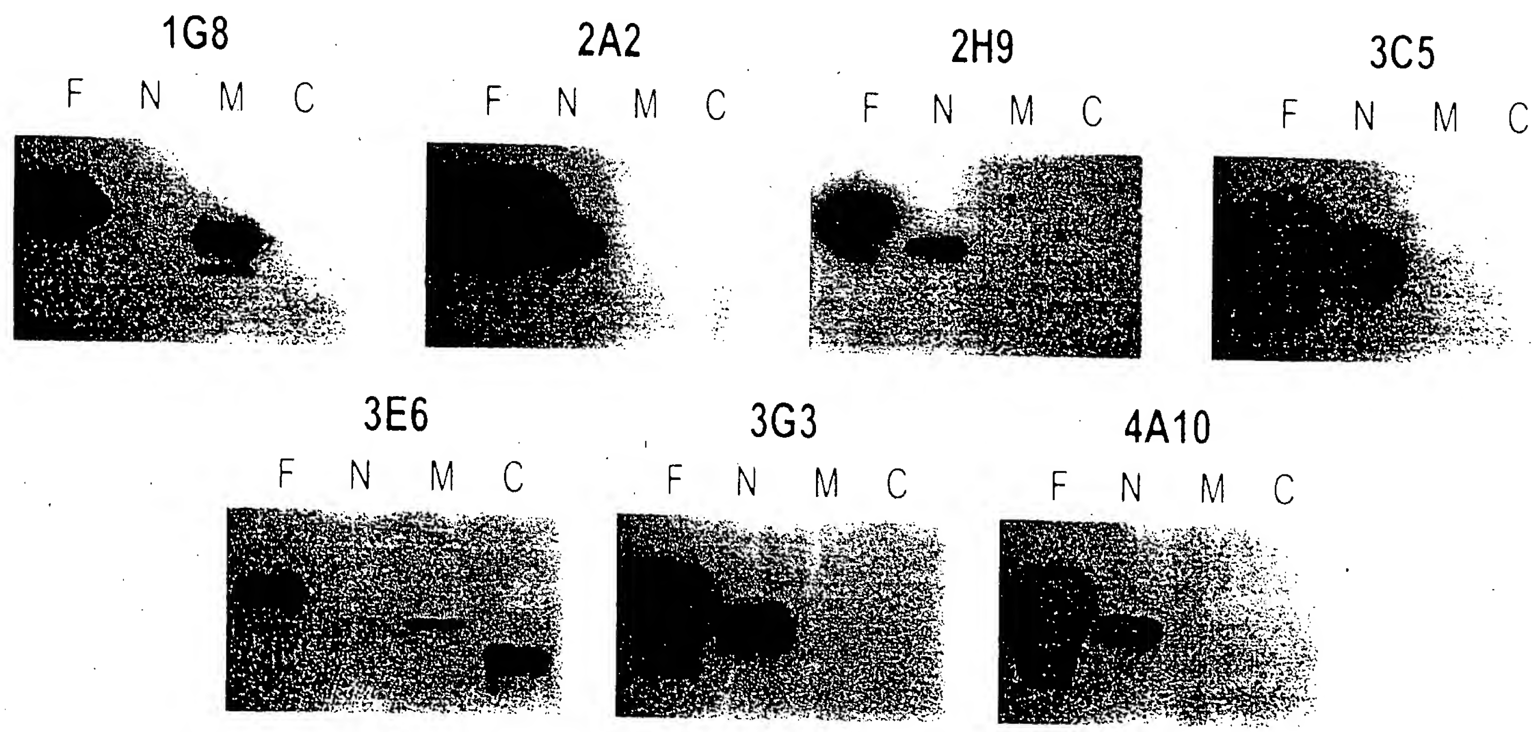


FIG. 50

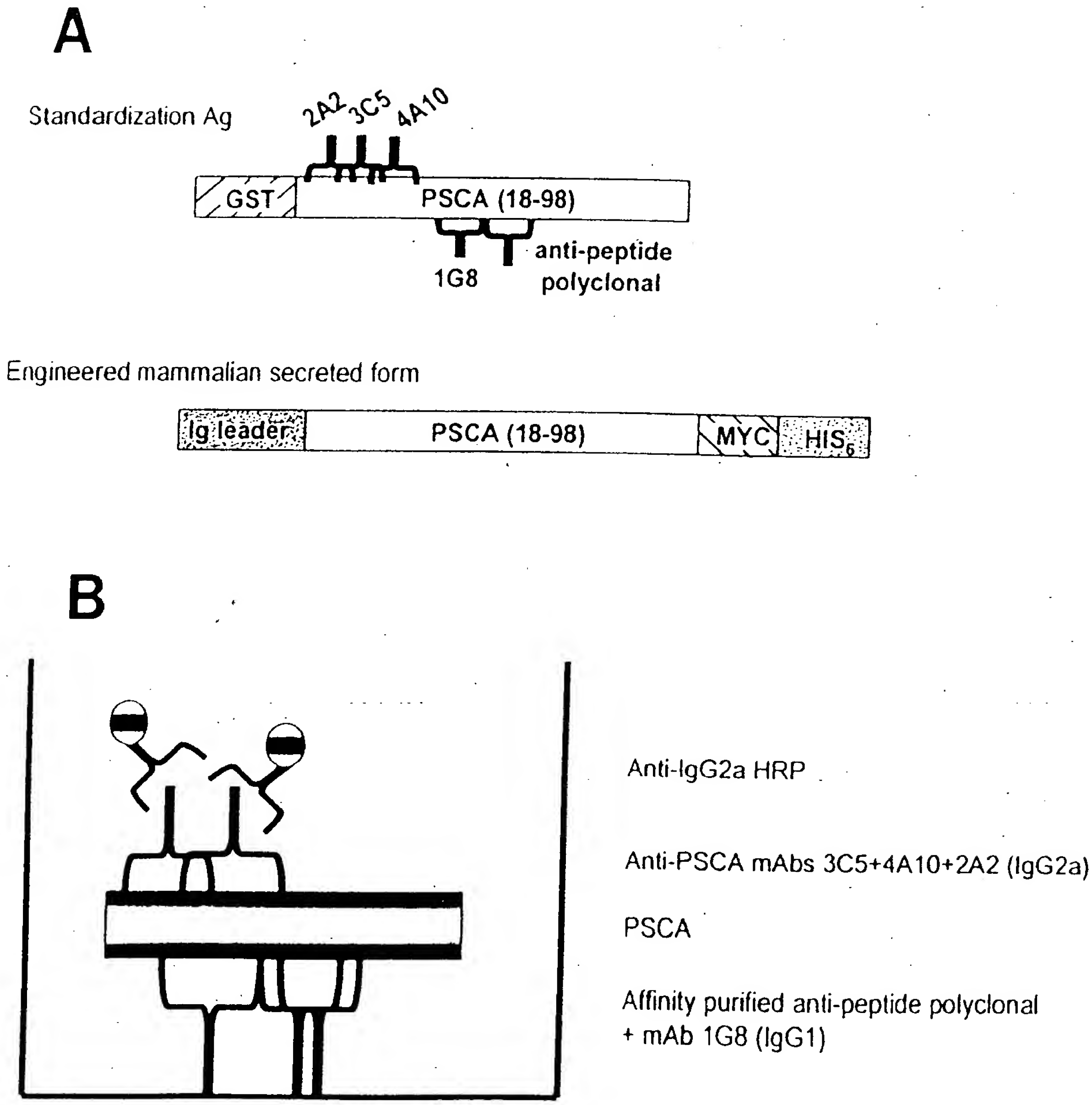
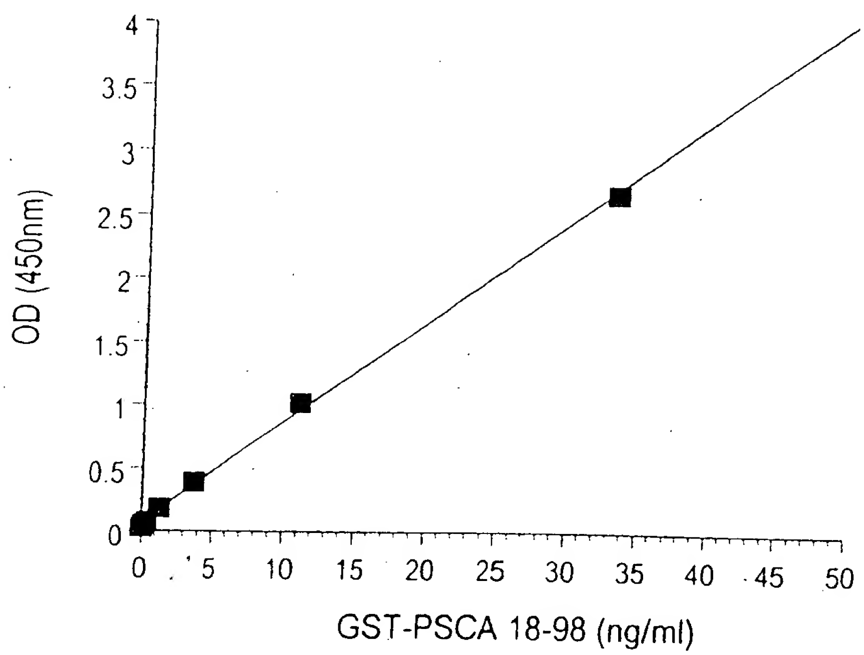

A
Standardization Ag
2A2
3C5
4A10
GST
PSCA (18-98)
anti-peptide polyclonal
1G8
Engineered mammalian secreted form
Ig leader
PSCA (18-98)
MYC
HIS6
B
Anti-IgG2a HRP
Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)
PSCA
Affinity purified anti-peptide polyclonal
+ mAb 1G8 (IgG1)

FIG. 51

A



B

Sample	OD+range (n=2)	ng/ml
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

09855632 .100901

FIG. 52

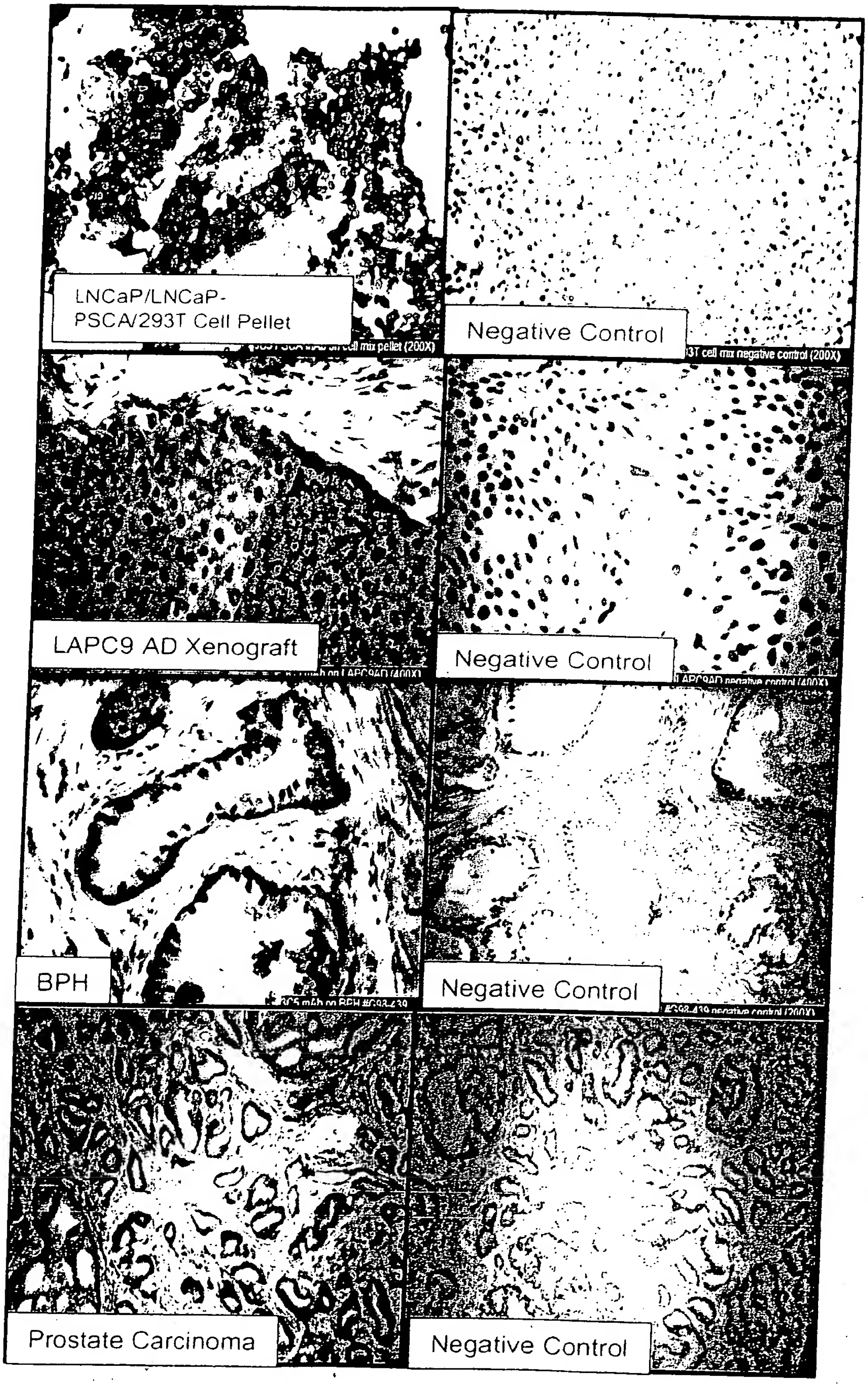
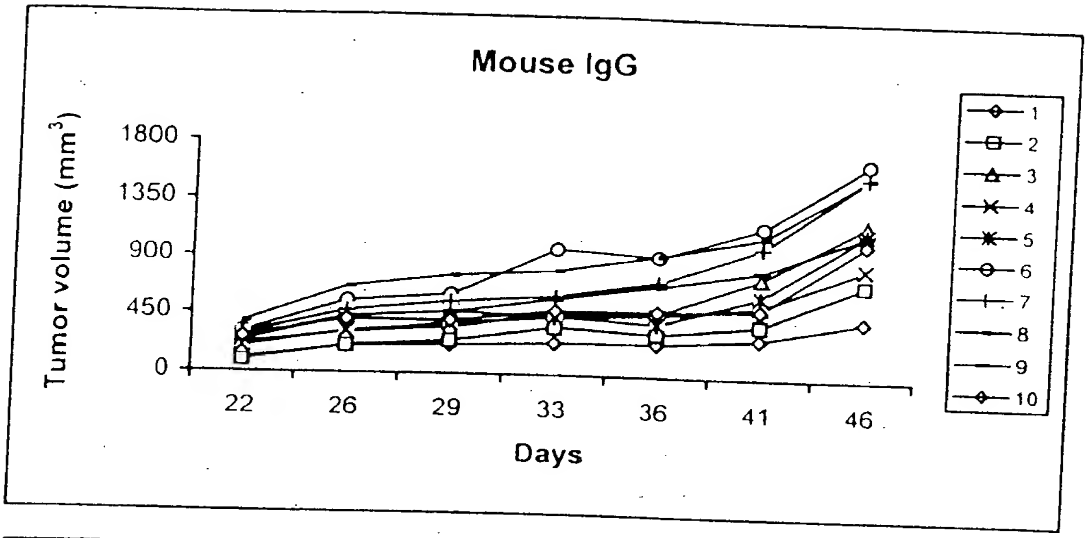
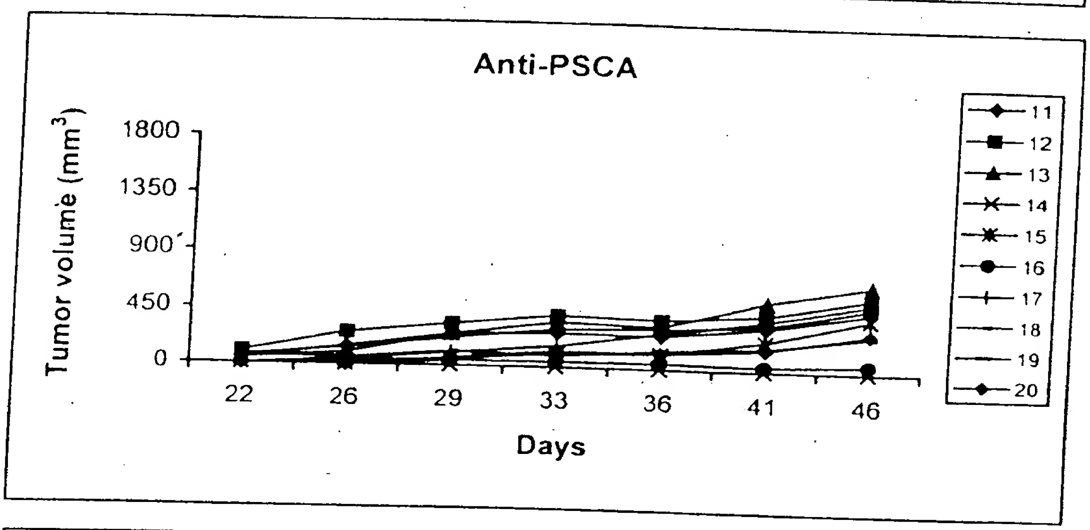


FIG. 53


Mouse IgG
Tumor volume (mm³)
1800
1350
900
450
0
22
26
29
33
36
41
46
Days
1
2
3
4
5
6
7
8
9
10


Anti-PSCA
Tumor volume (mm³)
1800
1350
900
450
0
22
26
29
33
36
41
46
Days
11
12
13
14
15
16
17
18
19
20

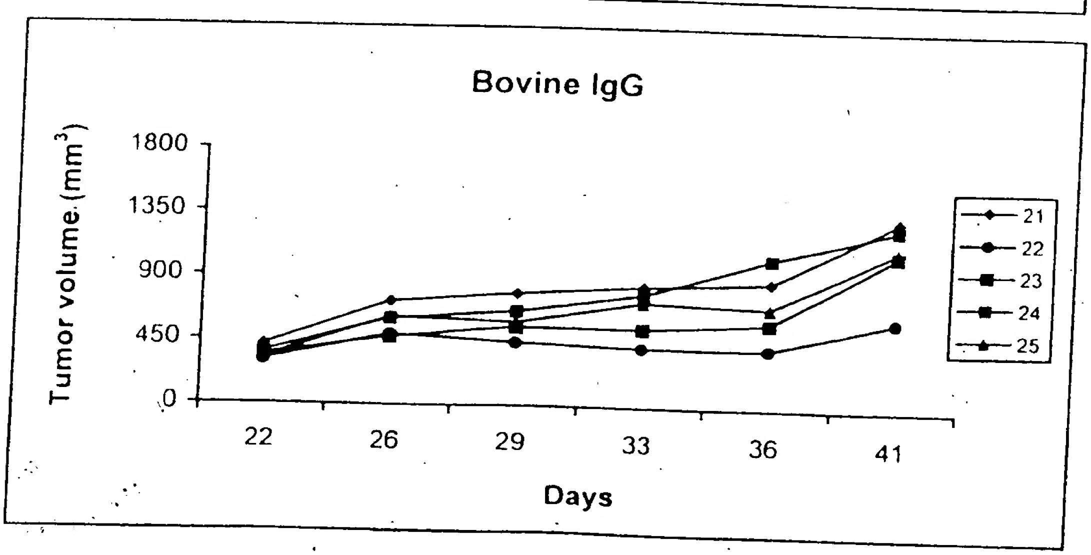

Bovine IgG
Tumor volume (mm³)
1800
1350
900
450
0
22
26
29
33
36
41
Days
21
22
23
24
25

FIG. 54

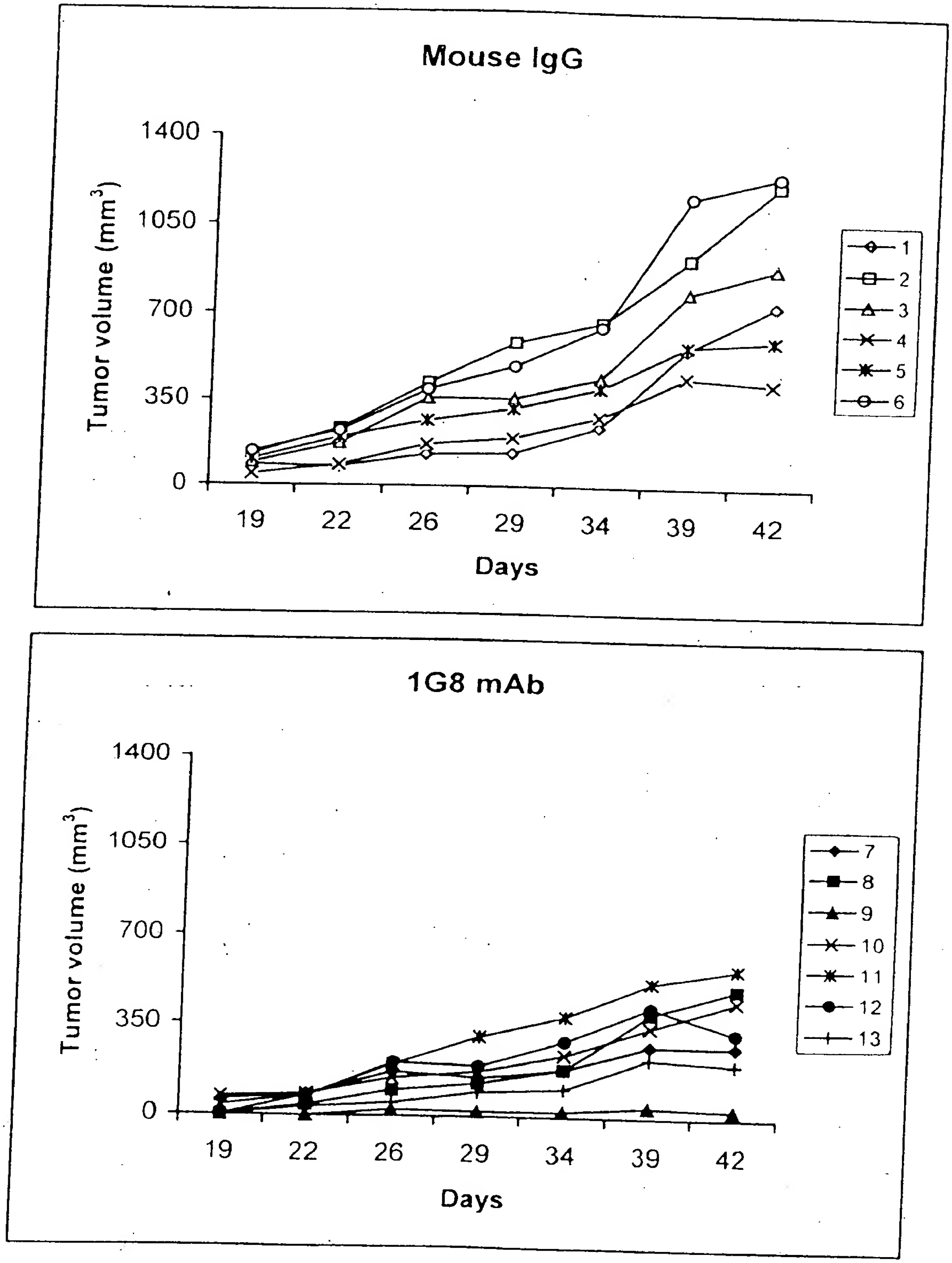
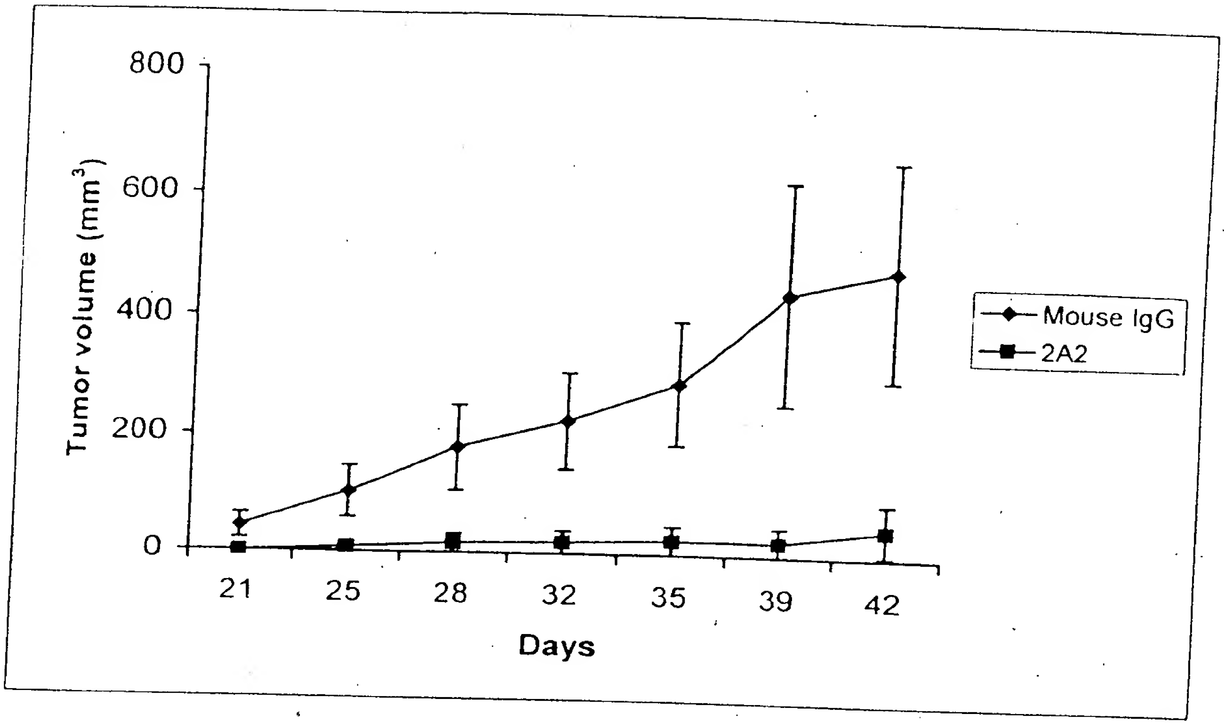

Mouse IgG
1400
1050
700
350
0
Tumor volume (mm3)
19
22
26
29
34
39
42
Days
1
2
3
4
5
6
1G8 mAb
1400
1050
700
350
0
Tumor volume (mm3)
19
22
26
29
34
39
42
Days
7
8
9
10
11
12
13

FIG. 55


800
600
400
200
0
Tumor volume (mm3)
21
25
28
32
35
39
42
Days
Mouse IgG
2A2

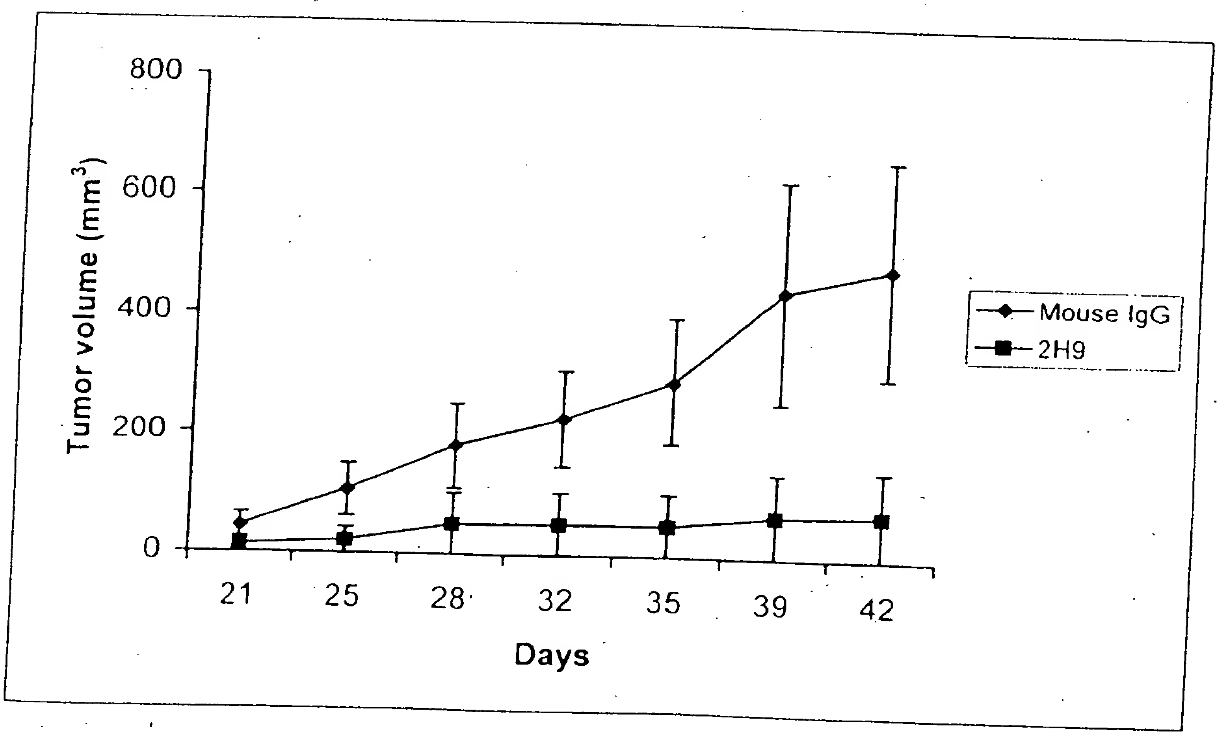
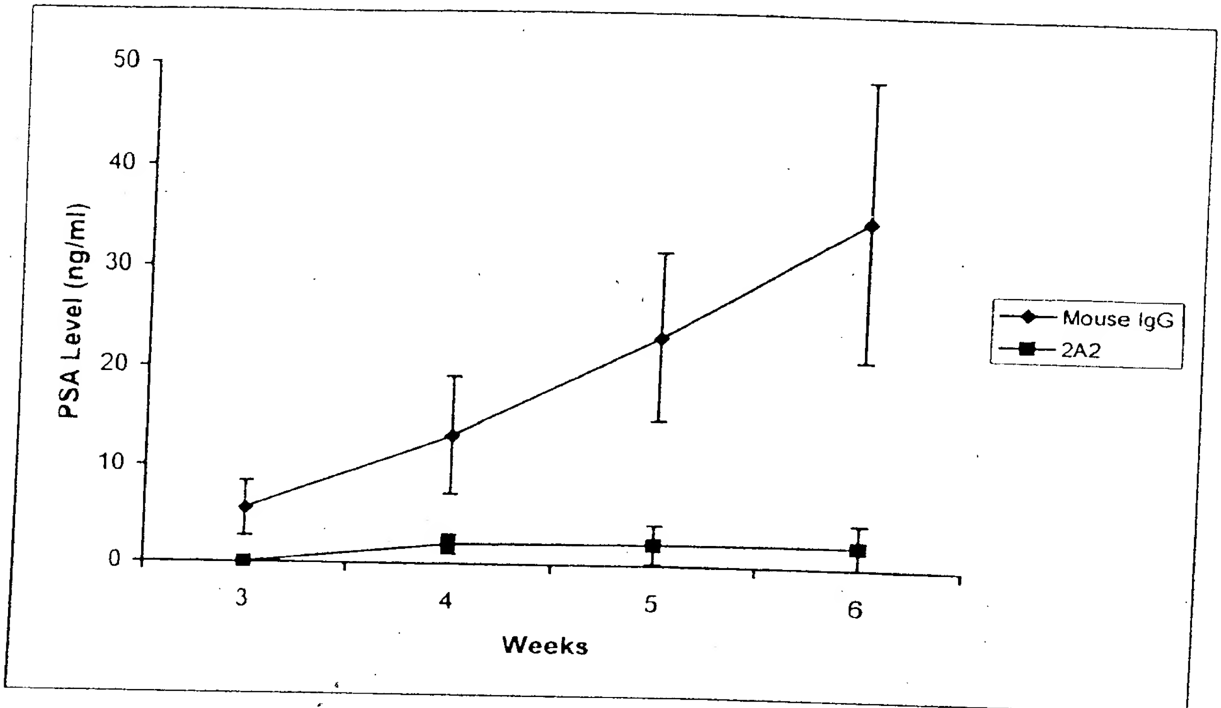

800
600
400
200
0
Tumor volume (mm3)
21
25
28
32
35
39
42
Days
Mouse IgG
2H9

FIG. 56


50
40
30
20
10
0
PSA Level (ng/ml)
3
4
5
6
Weeks
Mouse IgG
2A2

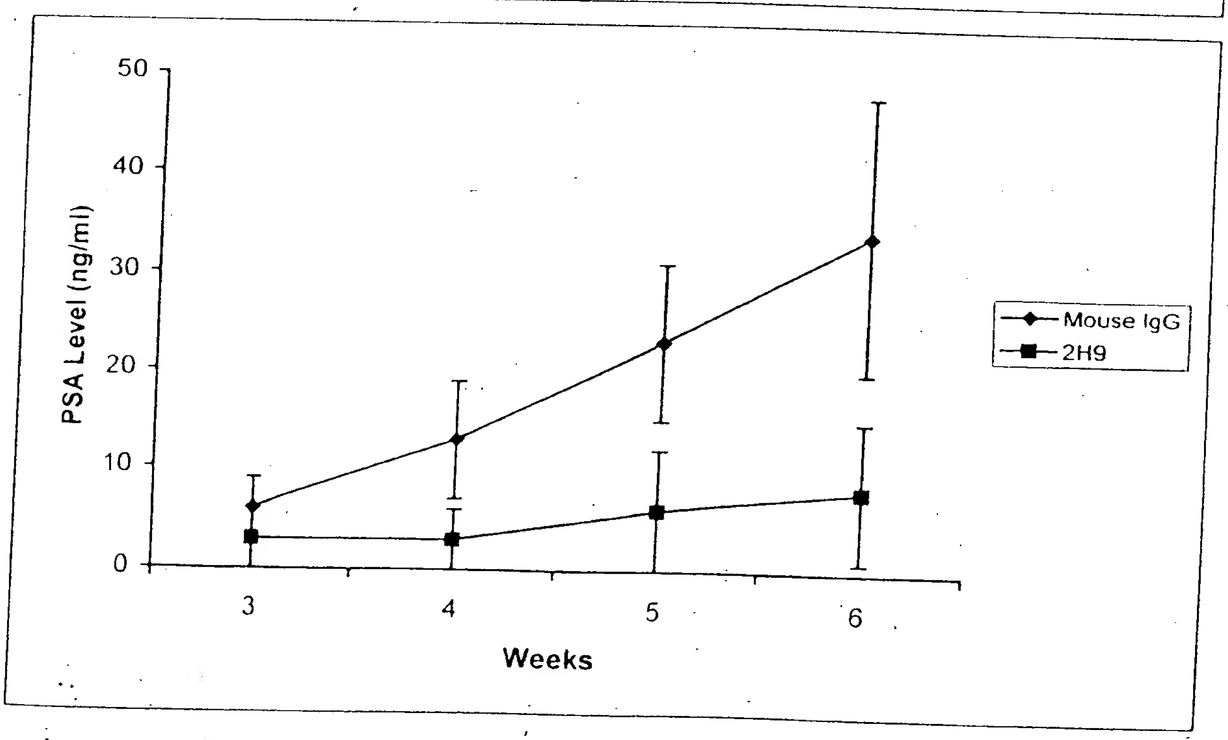
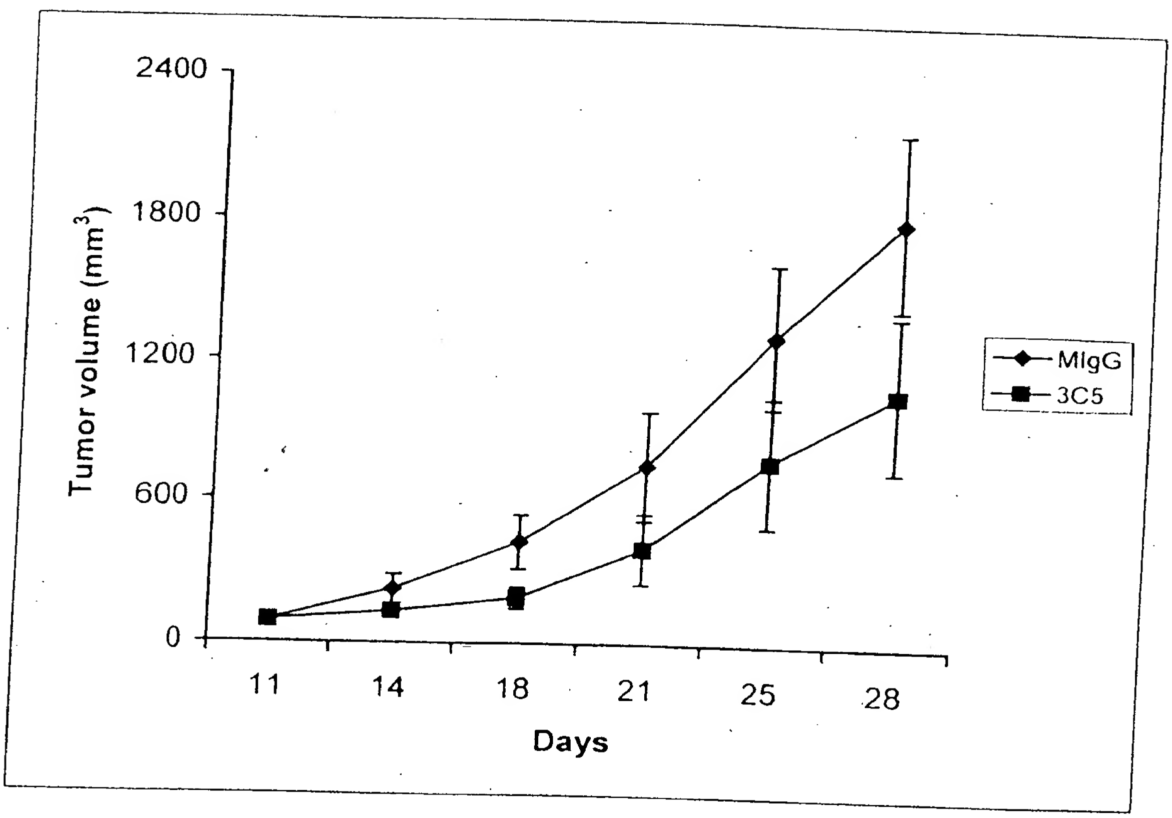

50
40
30
20
10
0
PSA Level (ng/ml)
3
4
5
6
Weeks
Mouse IgG
2H9

FIG. 57



2400
1800
1200
600
0
Tumor volume (mm3)
11
14
18
21
25
28
Days
MIgG
3C5

FIG. 58

```
TGCTTCTTCCTGATGGCAGTGGTTATAGGAGTCAATTCAGAGGTTCAGCTGCAGCAGTCT  60
 C  F  F  L  M  A  V  V  I  G  V  N  S  E  V  Q  L  Q  Q  S   20

GGGGCAGAACTTGTGAGGTCAGGGGCCTCAGTCAAGTTGTCCTGCACAGCTTCTGGCTTC 120
 G  A  E  L  V  R  S  G  A  S  V  K  L  S  C  T  A  S  G  F   40

            CDR1
AACATTAAAGACTACTATATACACTGGGTGAATCAGAGGCCTGACCAGGGCCTGGAGTGG 180
 N  I  K  D  Y  Y  I  H  W  V  N  Q  R  P  D  Q  G  L  E  W   60

                        CDR2
ATTGGATGGATTGATCCTGAGAATGGTGACACTGAATTTGTCCCGAAGTTCCAGGGCAAG 240
 I  G  W  I  D  P  E  N  G  D  T  E  F  V  P  K  F  Q  G  K   80

GCCACTATGACTGCAGACATTTTCTCCAACACAGCCTACCTGCACCTCAGCAGCCTGACA 300
 A  T  M  T  A  D  I  F  S  N  T  A  Y  L  H  L  S  S  L  T  100

                                   CDR3
TCTGAAGACACTGCCGTCTATTACTGTAAAACGGGGGGTTTCTGGGGCCAAGGGACTCTG 360
 S  E  D  T  A  V  Y  Y  C  K  T  G  G  F  W  G  Q  G  T  L  120

GTCACTGTCTCTGCAGCCAAAACGACACCCCCATCTGTCTATCCACTG
 V  T  V  S  A  A  K  T  T  P  P  S  V  Y  P  L
```

FIG. 59

```
TTGGTAGCAACAGCCTCAGATGTCCACTCCCAGGTCCAACTGCAGCAACCTGGGTCTGAA  60
 L  V  A  T  A  S  D  V  H  S  Q  V  Q  L  Q  Q  P  G  S  E   20

CTGGTGAGGCCTGGAACTTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTATACATTCTCC 120
 L  V  R  P  G  T  S  V  K  L  S  C  K  A  S  G  Y  T  F  S   40
                                                    CDR1

AGCTACTGGATGCACTGGGTGAAGCAGAGGCCTGGACAAGGCCTTGAGTGGATTGGAAAT 180
 S  Y  W  M  H  W  V  K  Q  R  P  G  Q  G  L  E  W  I  G  N   60

ATTGACCCTGGTAGTGGTTACACTAACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240
 I  D  P  G  S  G  Y  T  N  Y  A  E  N  L  K  T  K  A  T  L   80
          CDR2

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300
 T  V  D  T  S  S  S  T  A  Y  M  Q  L  S  S  L  T  S  E  D  100

TCTGCAGTCTATTACTGTACAAGCCGATCTACTATGATTACGACGGGATTTGCTTACTGG 360
 S  A  V  Y  Y  C  T  S  R  S  T  M  I  T  T  G  F  A  Y  W  120
                                   CDR3

GGCCAAGGGACTCTGGTCACTGTCTCTGCAGCTACAACAACAGCCCCATCTGTCTATCCA 420
 G  Q  G  T  L  V  T  V  S  A  A  T  T  T  A  P  S  V  Y  P  160

CTGGCC
 L  A
```

FIG. 60

```
AATGACTTCGGGTTGAGCTGGGTTTTTATTATTGTTCTTTTAAAAGGGGTCCGGAGTGAA  60
 N  D  F  G  L  S  W  V  F  I  I  V  L  L  K  G  V  R  S  E   20

GTGAGGCTTGAGGAGTCTGGAGGAGGCTGGGTGCAACCTGGAGGATCCATGAAACTCTCC 120
 V  R  L  E  E  S  G  G  G  W  V  Q  P  G  G  S  M  K  L  S   40

TGTGTAGCCTCTGGATTTACTTTCAGTAATTACTGGATGACTTGGGTCCGCCAGTCTCCA 180
 C  V  A  S  G  F  T  F  S  N  Y  W  M  T  W  V  R  Q  S  P   60
             ____________CDR1____________

GAGAAGGGGCTTGAGTGGGTTGCTGAAATTCGATTGAGATCTGAAAATTATGCAACACAT 240
 E  K  G  L  E  W  V  A  E  I  R  L  R  S  E  N  Y  A  T  H   80
                         _____________CDR2______________

TATGCGGAGTCTGTGAAAGGGAAATTCACCATCTCAAGAGATGATTCCAGAAGTCGTCTC 300
 Y  A  E  S  V  K  G  K  F  T  I  S  R  D  D  S  R  S  R  L  100
 ____________________

TACCTGCAAATGAACAACTTAAGACCTGAAGACAGTGGAATTTATTACTGTACAGATGGT 360
 Y  L  Q  M  N  N  L  R  P  E  D  S  G  I  Y  Y  C  T  D  G  120
                                                          _

CTGGGACGACCTAACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACA 420
 L  G  R  P  N  W  G  Q  G  T  L  V  T  V  S  A  A  K  T  T  140
 _____CDR3_____

CCCCCATCTGTCTATCCACTGGCCCCTTGTGTA
 P  P  S  V  Y  P  L  A  P  C  V
```

FIG. 61

CDR1 Comparisons

1G8	IgG$_{1k}$	Middle	G	F	N	I	K	D	Y	Y	I	H
2H9	IgG$_{1k}$	N-Term.	G	F	T	F	S	N	Y	W	M	T
4A10	IgG$_{2ak}$	N-Term.	G	Y	T	F	S	S	Y	W	M	H

CDR2 Comparisons

1G8	IgG$_{1k}$	W	I	D	P	E	N	G	D	T	E	F	V	P	K	F	Q	G		
2H9	IgG$_{1k}$	E	I	R	L	R	S	E	N	Y	A	T	H	Y	A	E	S	V	K	G
4A10	IgG$_{2ak}$	N	I	D	P	G	S	G	Y	T	N			Y	A	E	N	L	K	T

CDR3 Comparisons

1G8	IgG$_{1k}$	G	G	F								
2H9	IgG$_{1k}$	L	G	R	P	N						
4A10	IgG$_{2ak}$	R	S	T	M	I	T	T	G	F	A	Y

FIG. 62

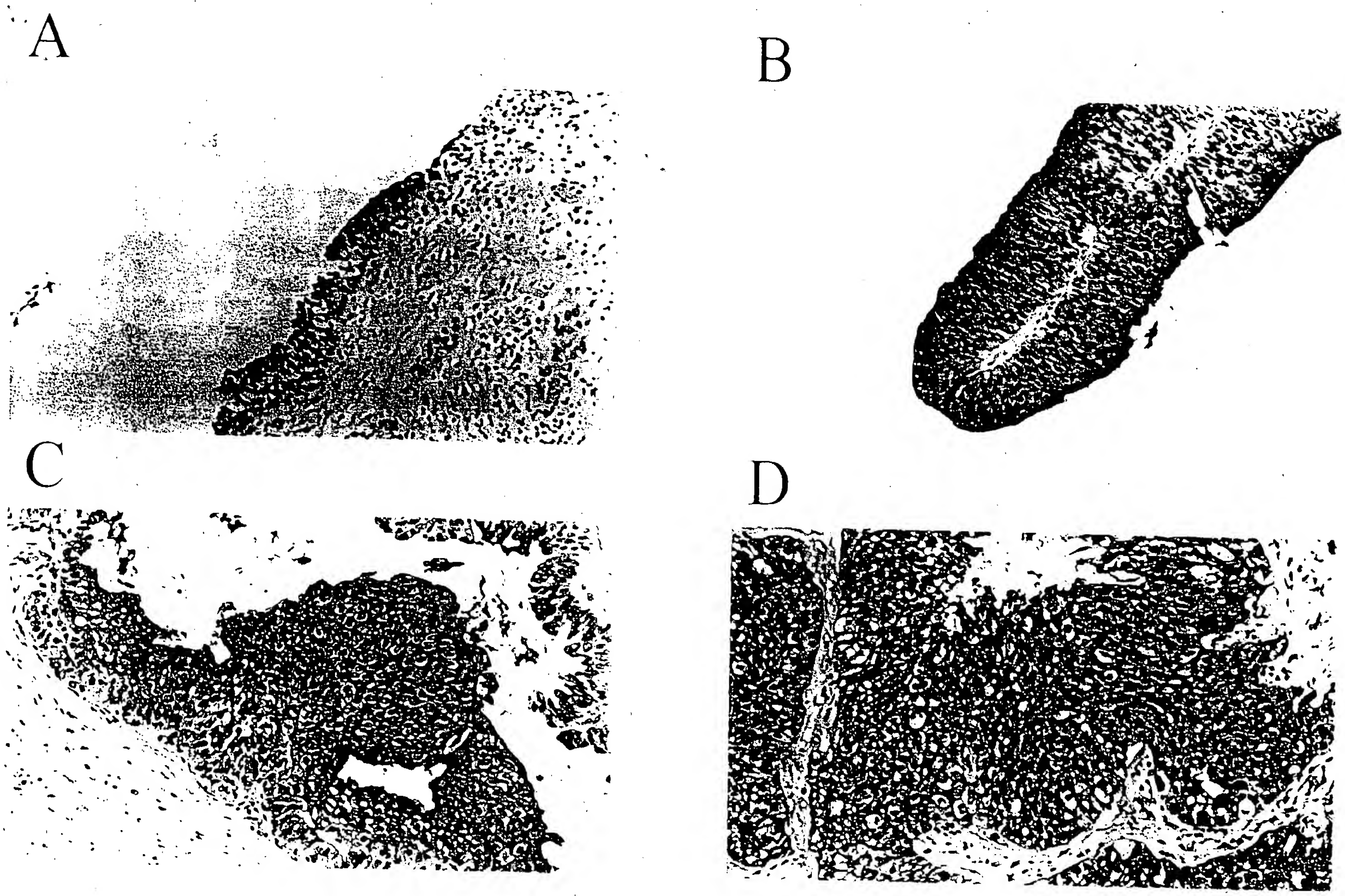
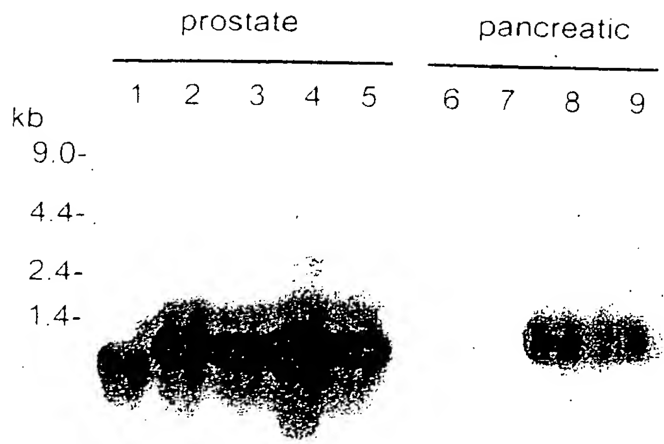
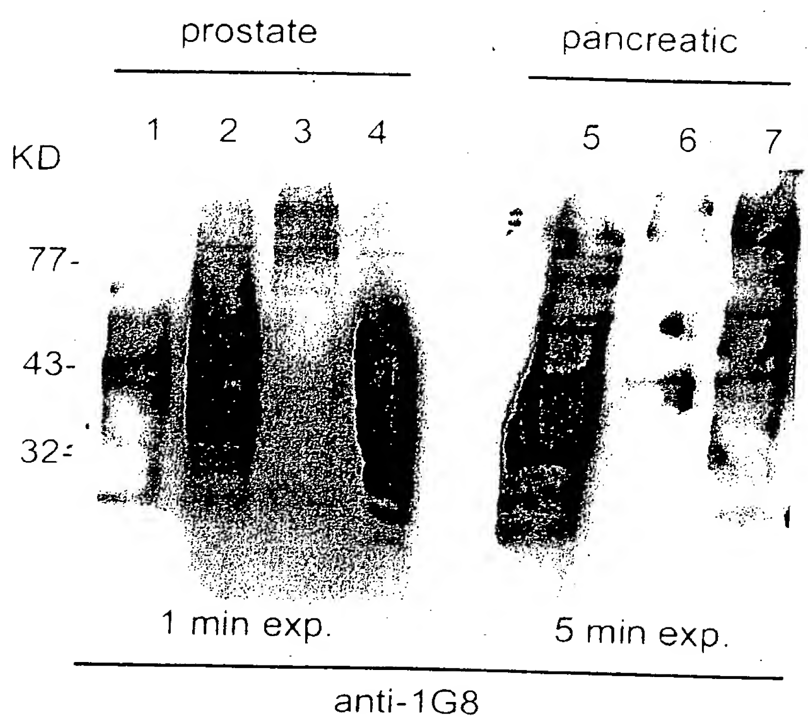


FIG. 63



1. Prostate
2. LAPC-4 AD
3. LAPC-4 AI
4. LAPC-9 AD
5. LAPC-9 AI
6. PANC-1
7. BxPC-3
8. HPAC
9. Capan-1

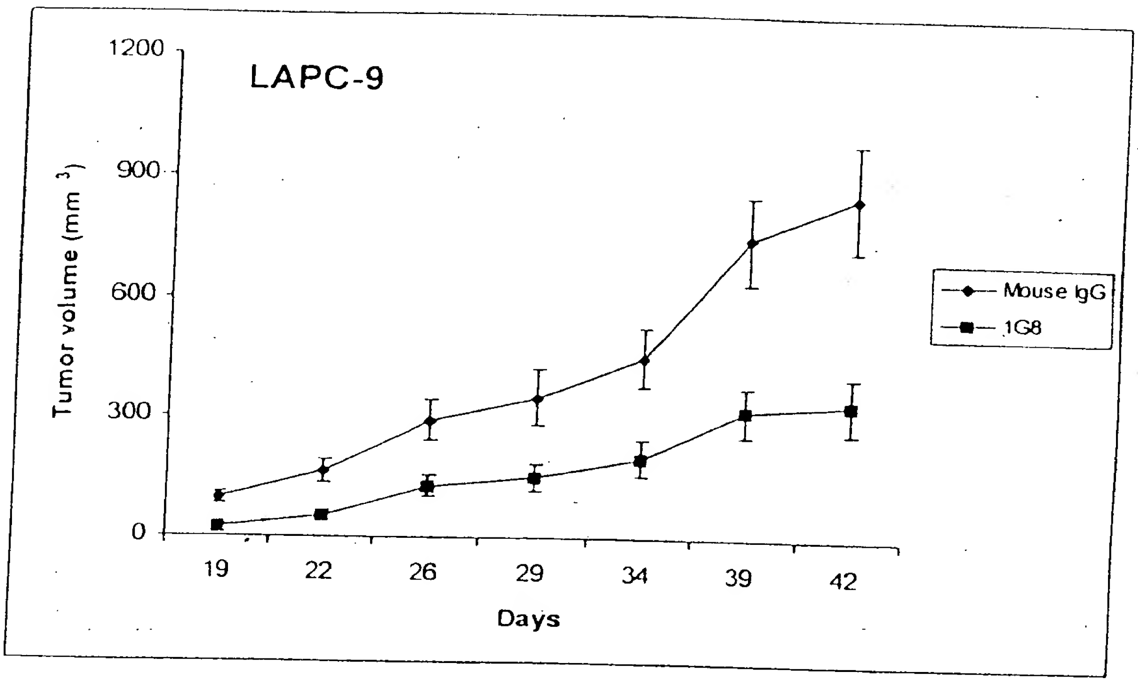
FIG. 64



1. LAPC-4 AD
2. LAPC-9 AI
3. LNCaP
4. LNCaP-PSCA

5. HPAC
6. Capan-1
7. ASPC-1

FIG. 65


LAPC-9
1200
900
600
300
0
Tumor volume (mm 3)
19
22
26
29
34
39
42
Days
Mouse IgG
1G8

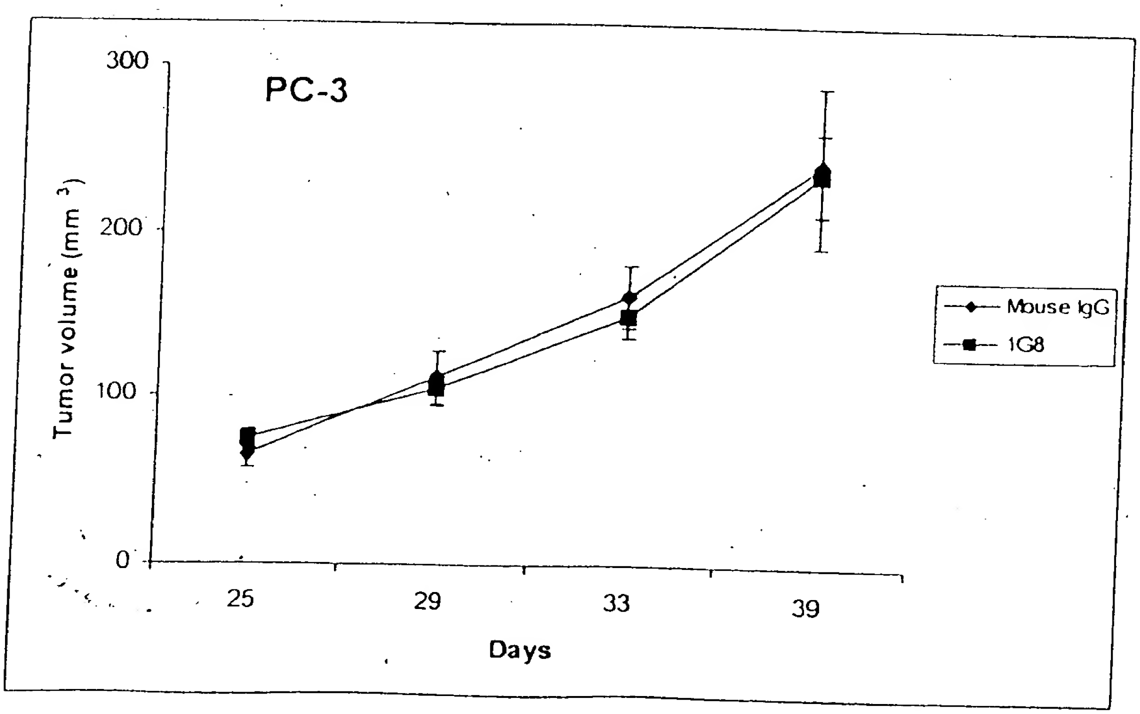
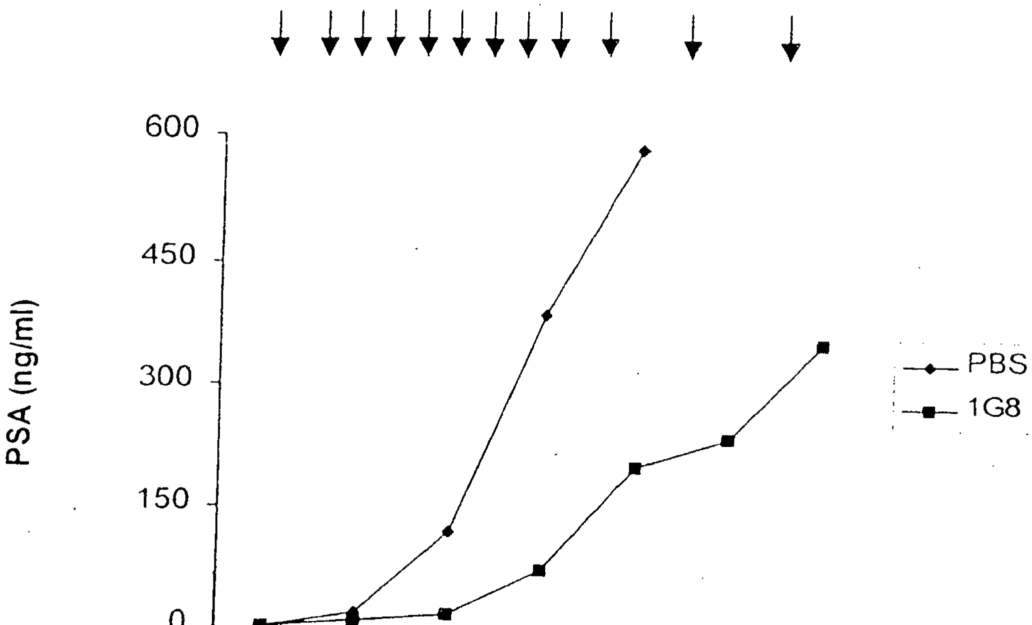

PC-3
300
200
100
0
Tumor volume (mm 3)
25
29
33
39
Days
Mouse IgG
1G8

FIG. 66

A)

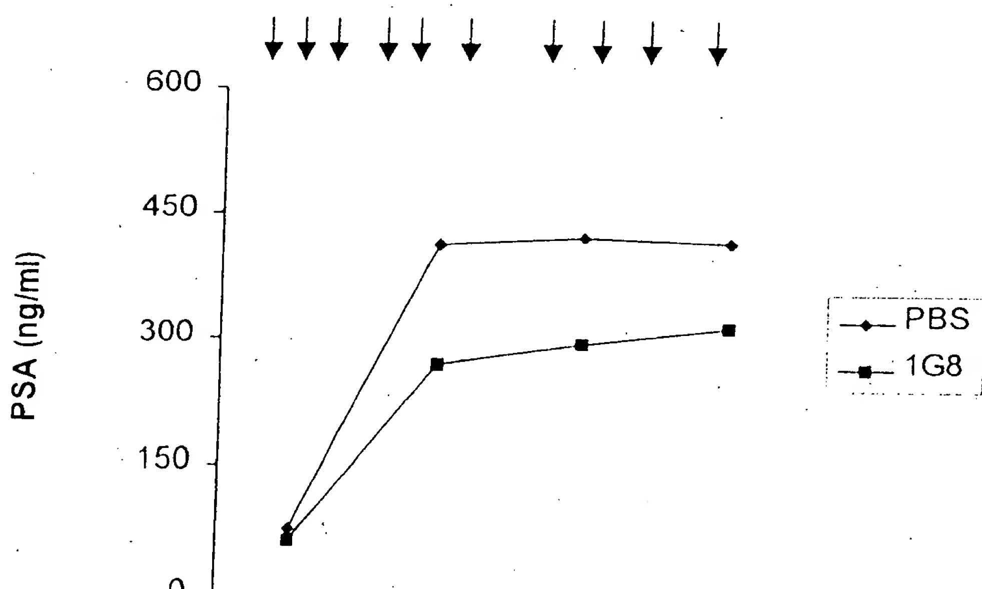


	9	15	22	30	37	44	51
PBS	2.3	20	119	386	583		
1G8	2.8	8.3	16.2	71	198	234	351

Mean PSA Levels (ng/ml)

Days

B)



	13	21	27	34
PBS	78	412	422	418
1G8	64	268	294	315

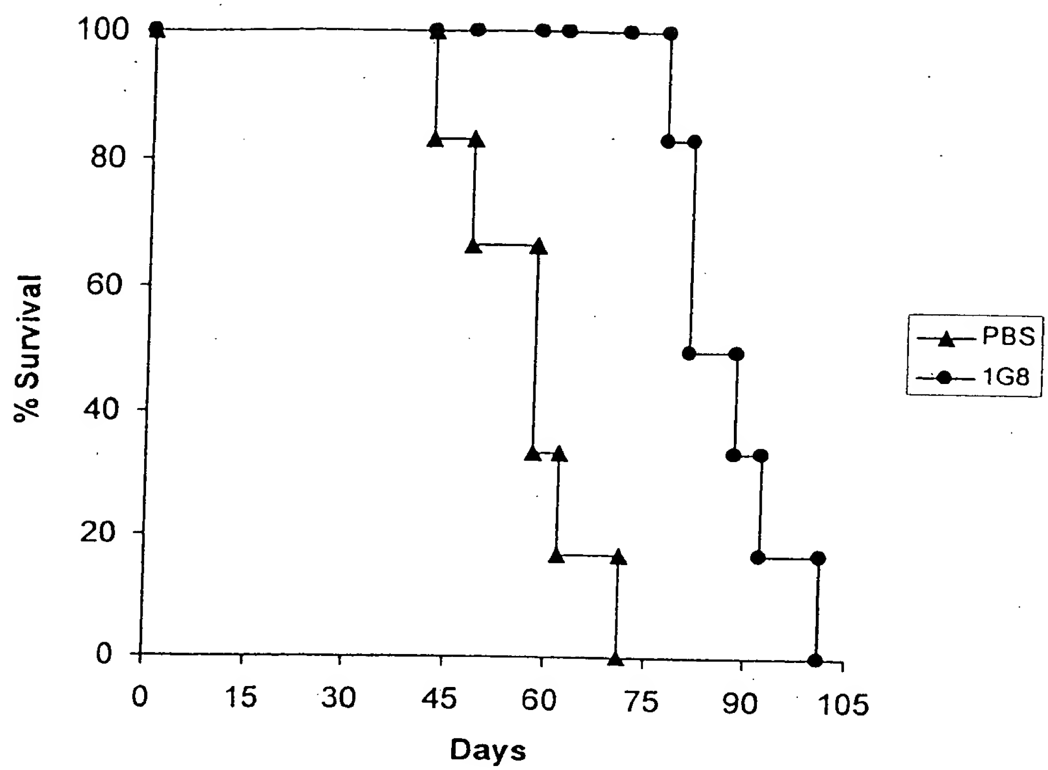
Mean PSA Levels (ng/ml)

Days

09855632.100901

F IG. 67

A)



B)

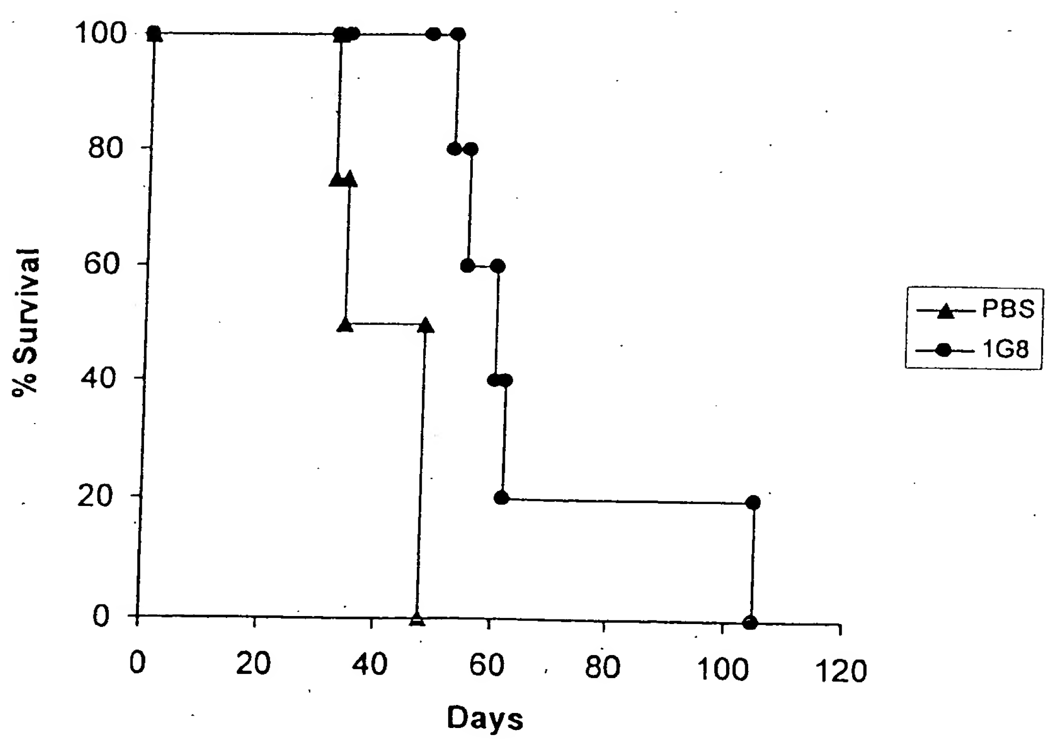
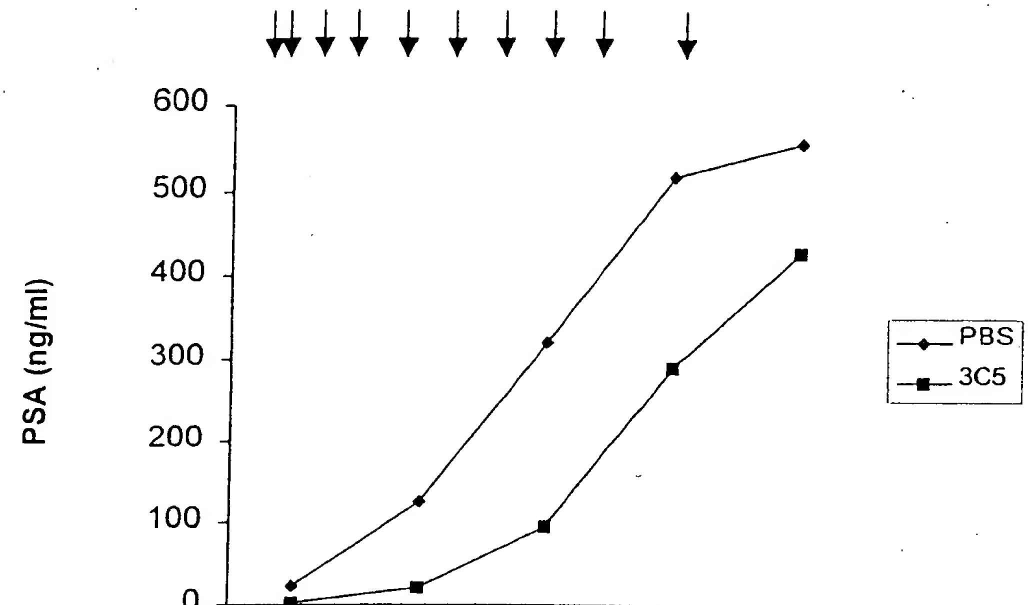


FIG. 68

A)

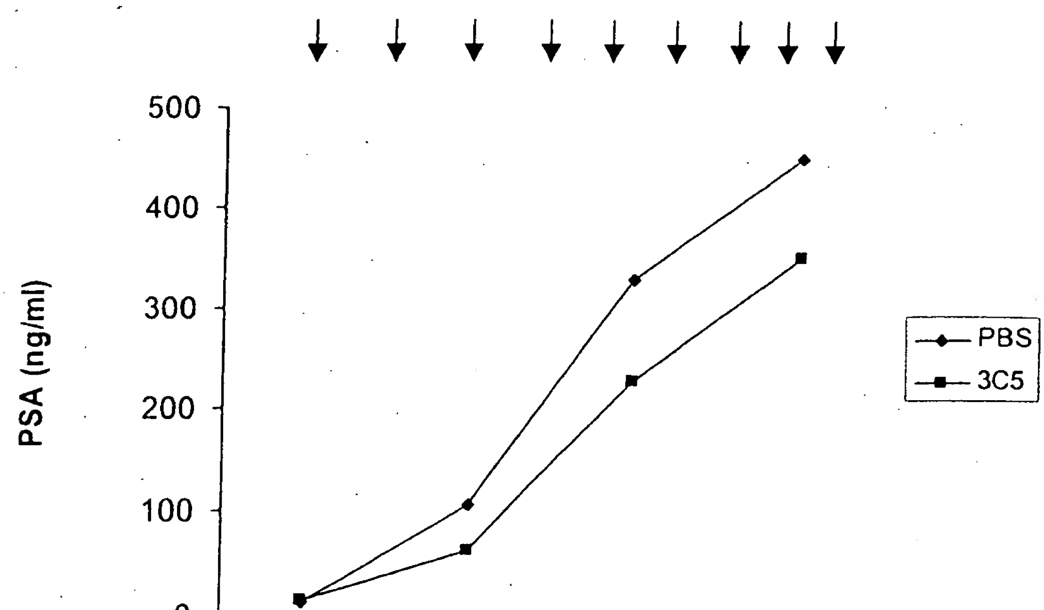


	9	16	22	29	36
PBS	23	126	322	519	555
3C5	3	21	95	290	428

Mean PSA Levels (ng/ml)

Days

B)



	7	14	21	28
PBS	14	107	329	449
3C5	16	63	229	351

Mean PSA Levels (ng/ml)

Days

FIG. 69

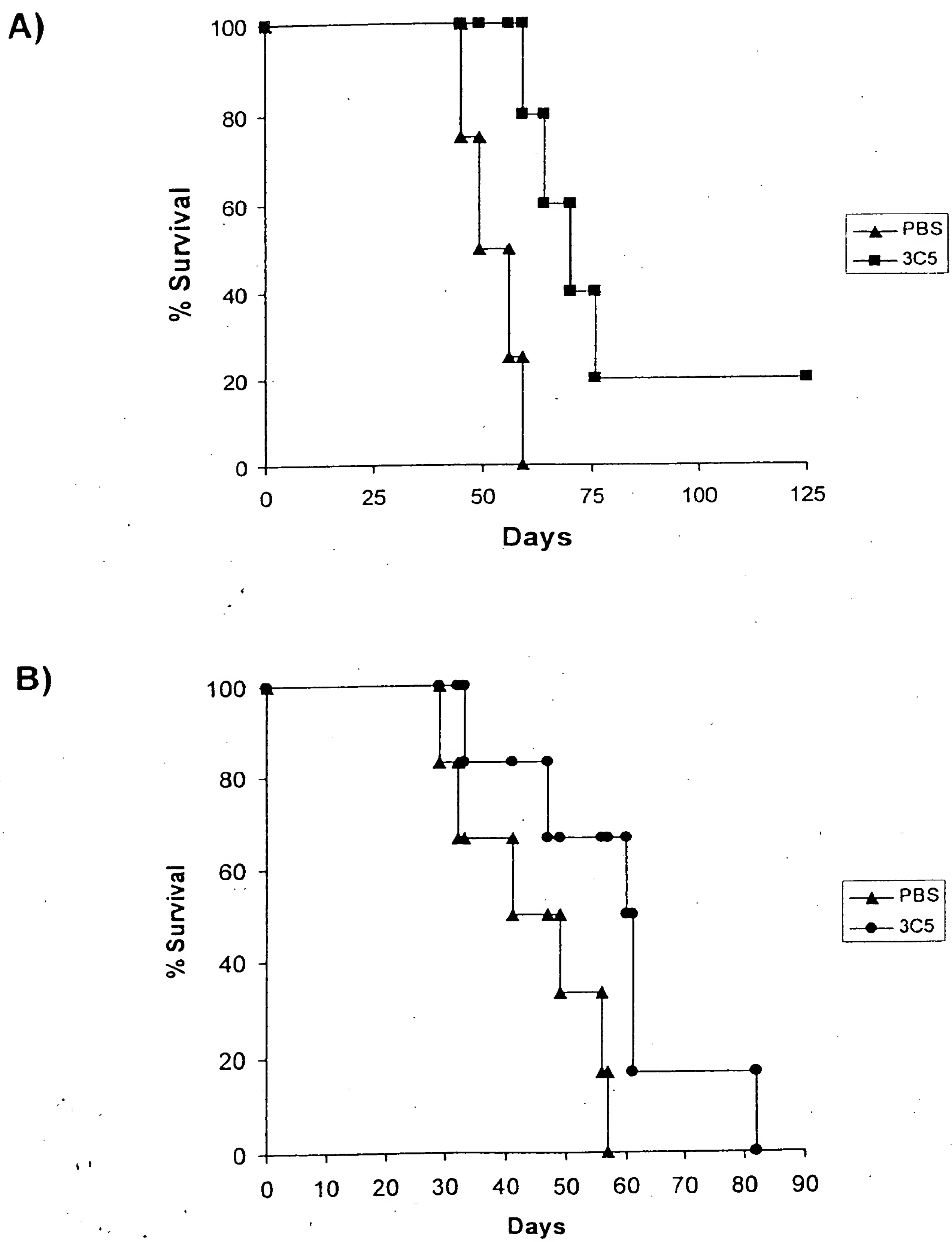
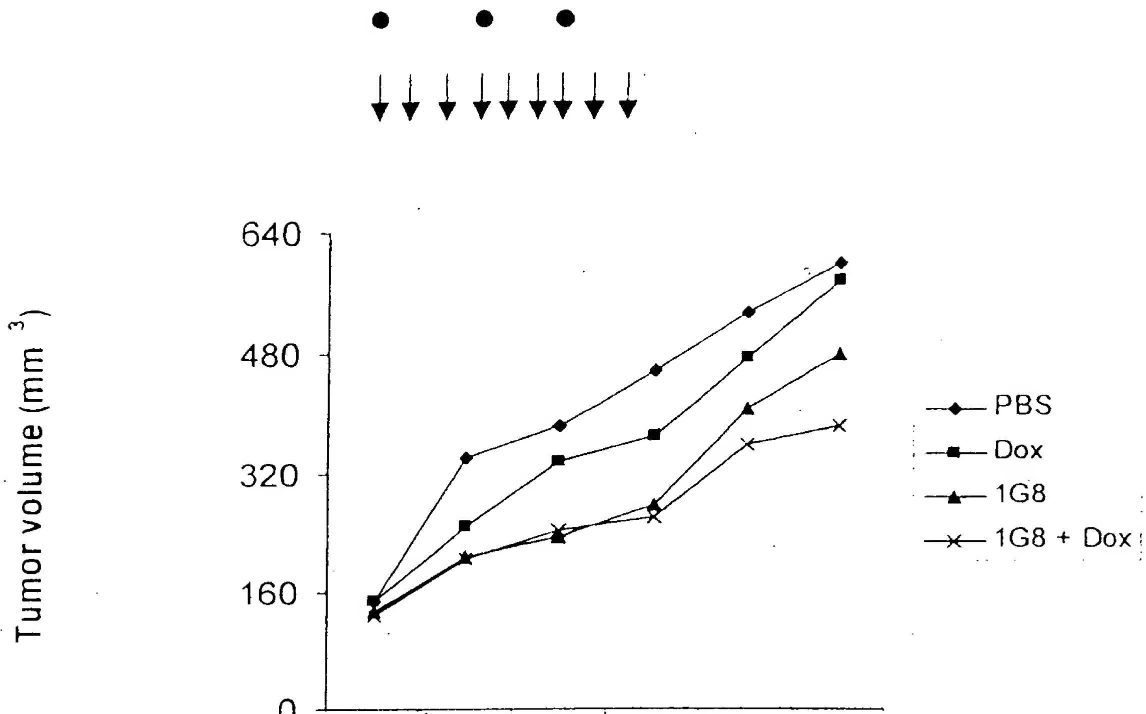

A)
100
80
60
40
20
0
% Survival
0
25
50
75
100
125
Days
PBS
3C5
B)
100
80
60
40
20
0
% Survival
0
10
20
30
40
50
60
70
80
90
Days
PBS
3C5

FIG. 70

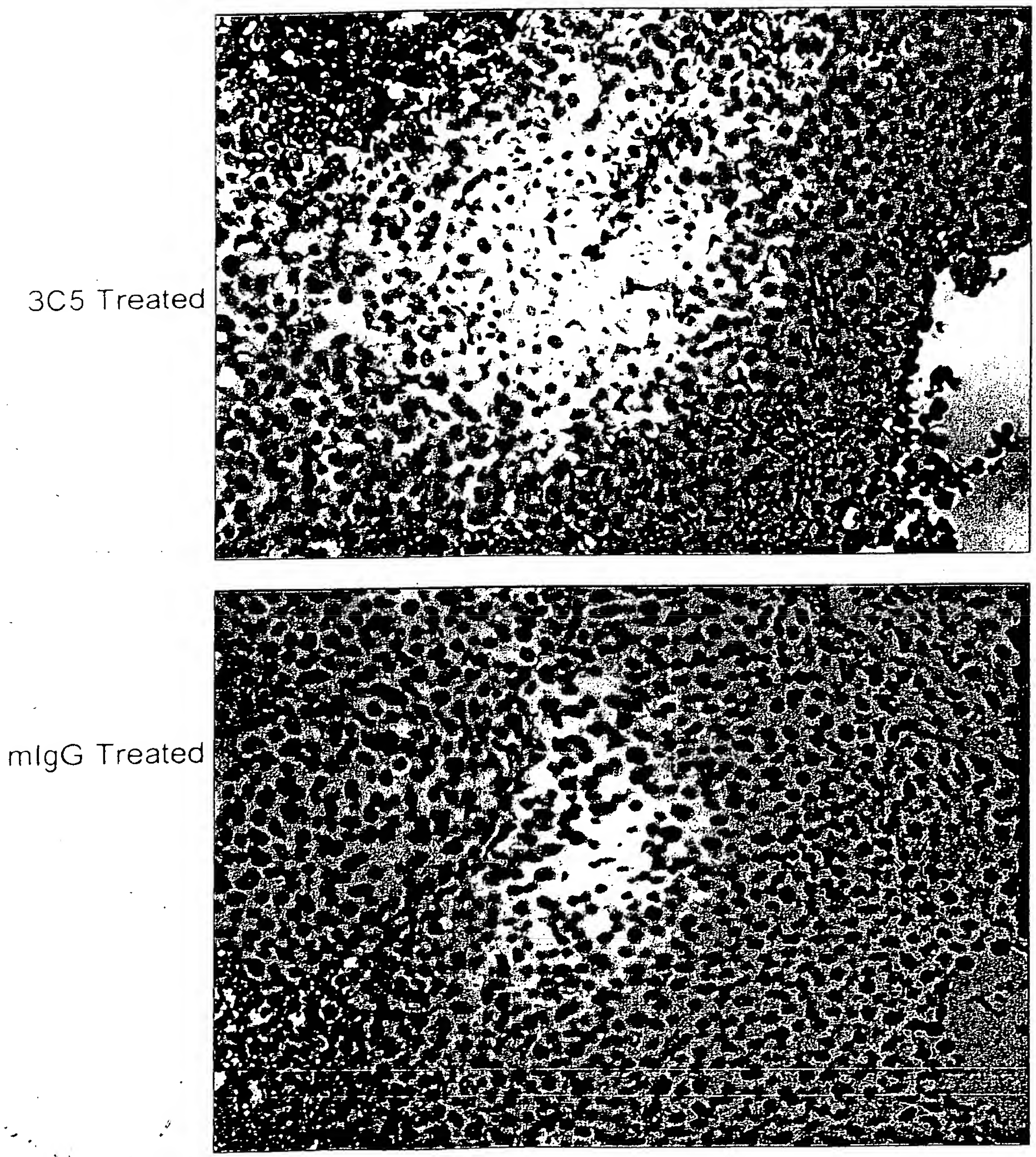


	9	15	23	29	36	43
PBS	149	343	385	458	533	601
Dox	148	250	337	371	473	577
1G8	135	208	235	276	408	479
1G8 + Dox	129	205	242	260	359	387

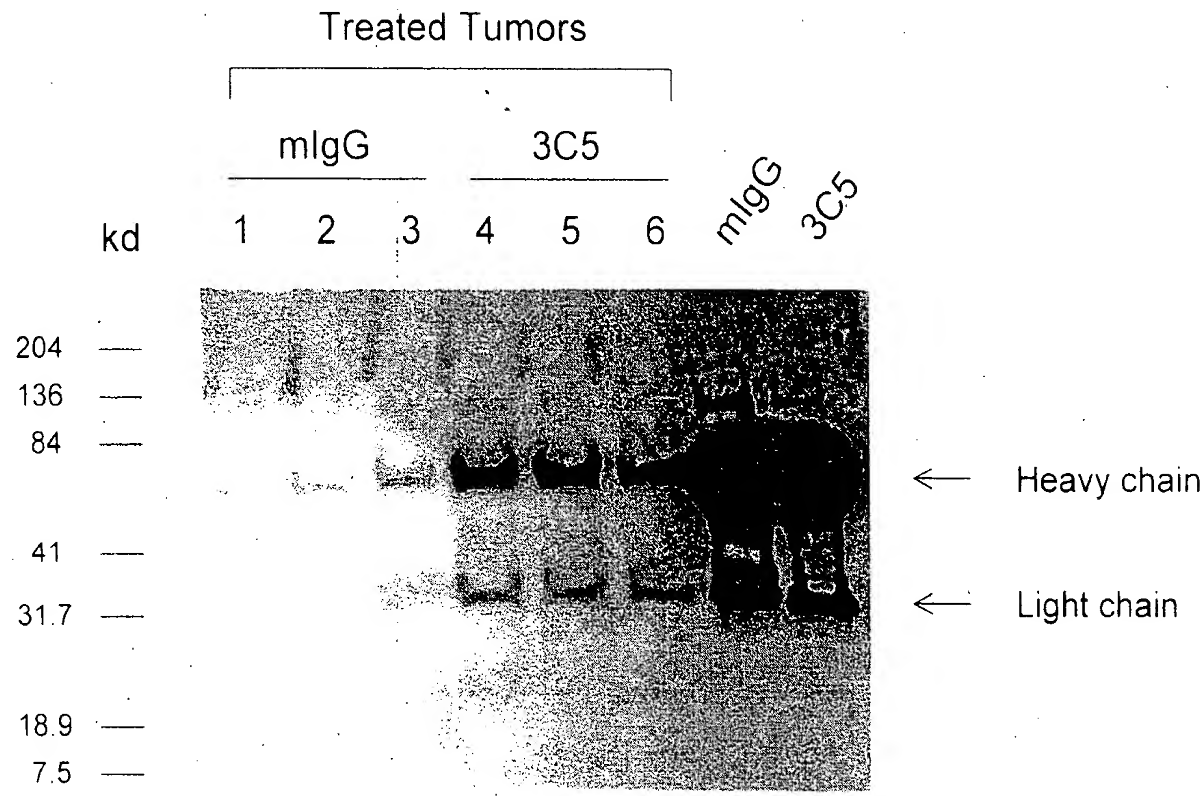
Days

FIG. 71

PSCA 3C5 MAb Localizes within LAPC9AD Xenograft Tissue



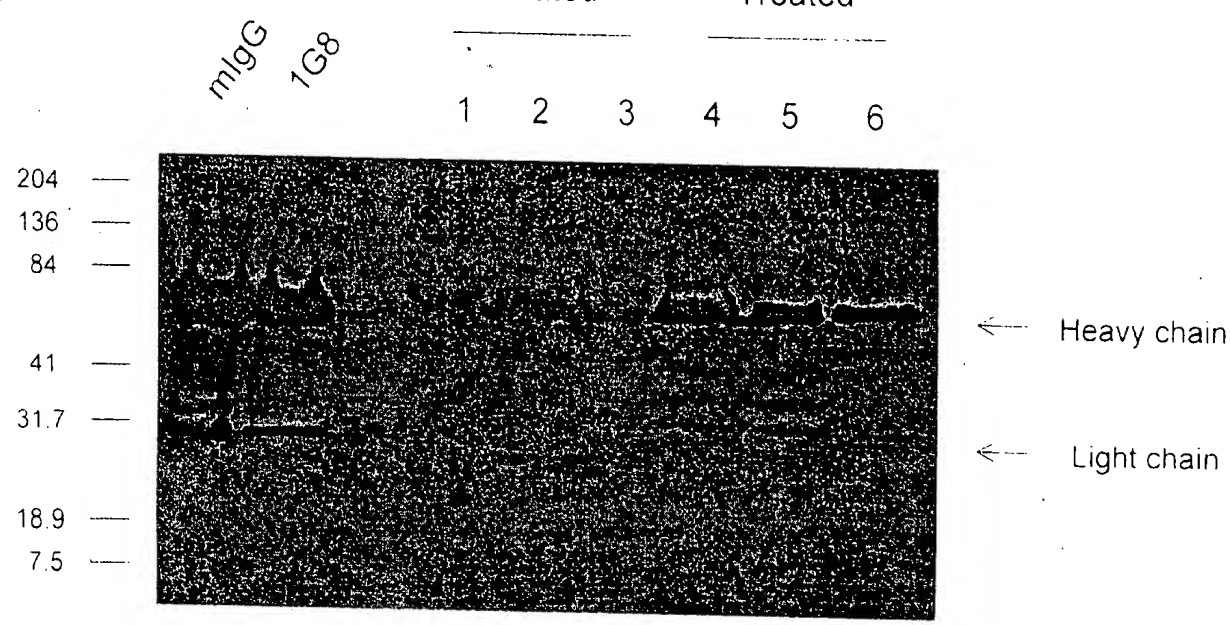
3C5 Anti-PSCA MAb is Localized to Established LAPC-9 Tumors



Western blot developed with α-mIgG/κ

FIG. 72

SPECIFIC TARGETING OF THE 1G8 ANTI-PSCA MAb TO ESTABLISHED LAPC-9 TUMORS



- α-MIgG Western

Method: Mice bearing established LAPC-9 tumors (>100 mm^3) were injected with either mIgG or the anti-PSCA MAb 1G8. Tumors were harvested a week later and made into protein lysates for Western analysis.

FIG. 73